D. Risk Factors

Any investment in our common stock or ADSs involves risk. Investors should carefully consider, in light of their own financial circumstances and investment objectives, the following risks before making an investment decision with respect to our common stock or ADSs. If any of the following risks actually occurs, it could have a material adverse effect on our business, financial condition, results of operations, future prospects, and the market value of our common stock or ADSs may be adversely affected.

The risks discussed below are those that we believe are material, but these risks and uncertainties may not be the only risks that we face. Additional risks that are not known to us at this time, or that are currently believed to be not material, could also have a material adverse effect on our business, financial condition, results of operations, future prospects and the market value of our common stock or ADSs.

Risks Relating to Our Business

We may fail to realize the anticipated benefits of the Shire Acquisition and expect to continue to record significant expenses related to it.

On January 8, 2019, we acquired the entire issued and to-be-issued share capital of Shire pursuant to a Scheme of Arrangement under the laws of Jersey (the "Shire Acquisition"). The ultimate success of the Shire Acquisition depends on our ability to realize the anticipated growth opportunities and synergies leading to cost savings we expect from combining the companies' businesses. We continue to devote significant time and resources to the reorganization of our personnel structure, enhancement of cost-efficiency and the strengthening of management and operational functions in order to realize the anticipated synergies of the Shire Acquisition. In connection with the integration of Shire, we incurred non-recurring cash costs totaling 1.85 billion USD in the fiscal year ended March 31, 2020 and expect to incur an additional 1.15 billion USD through the fiscal year ending March 31, 2022.

Furthermore, in connection with the Shire Acquisition, we recognized significant non-cash expenses relating to the unwinding of fair value adjustments to inventory as a component of cost of sales in the fiscal years ended March 31, 2019 and 2020 and expect that we will continue to incur a certain level of such expenses in future fiscal years. We also recorded significant intangible assets in connection with the Shire Acquisition and, as a result, amortization increased significantly in the fiscal years ended March 31, 2019 and 2020 and we expect to continue to record significant amounts of amortization expense in future fiscal years.

We recorded significant amounts of goodwill in connection with the Shire Acquisition, and, if we are unable to achieve the anticipated benefits of this acquisition, we could be required to recognize significant impairment losses related to such goodwill and to intangible assets recorded in connection with the acquisition, potentially up to their full value.

The expected synergies of the Shire Acquisition and the projected cash costs necessary to achieve the synergies may be affected by changes in the overall economic, political and regulatory environment, including applicable tax regimes and fluctuations in foreign exchange rates, and the realization of the other risks relating to our business described herein. Furthermore, the integration process may divert management's attention from other strategic opportunities and the day-to-day operation of our business. If we are not able to successfully manage the integration process, the anticipated benefits of the acquisition and subsequent integration may not be realized fully or at all or may take longer or prove more costly to realize than expected.

Although integration activities are underway, we may face significant challenges in integrating the organizations, business cultures, procedures and operations of Takeda and Shire, including:

- integrating operations and systems, such as research and development, manufacturing, distribution, marketing and promotional activities and information technology systems, while maintaining focus on selling and promoting existing and newly acquired or produced products;
- inability to realize expected benefits from newly acquired or produced products, including pipeline products under development;
- coordinating and integrating geographically dispersed organizations;
- changes or conflicts in the standards, controls, procedures and accounting and other policies, as well as business cultures and compensation structures;
- maintaining and growing Shire's customer base;
- incremental tax exposure based on the differences in our corporate structure and Shire's, including the exposure of each of the legacy Takeda businesses and the legacy Shire businesses to new tax regimes, particularly, in the case of Shire, to Japanese tax rules;
- maintaining business relationships with suppliers, third-party alliance partners and other key counterparties; and
- inefficiencies associated with the integration of the operations of the two companies.

Additionally, because we issued a significant number of additional shares of our common stock as part of the consideration for the Shire Acquisition, a failure to achieve the anticipated benefits of the Shire Acquisition could negatively affect our earnings per share.

We have substantial debt, including a significant amount incurred in connection with the Shire Acquisition, which may limit our ability to execute our business strategy, refinance existing debt or incur new debt, and if we are unable to meet our goals for deleveraging, we could be at a greater risk of a downgrade of our credit ratings.

Our consolidated bonds and loans were 5,093.3 billion JPY as of March 31, 2020, the majority of which was incurred in connection with the Shire Acquisition or represents indebtedness of Shire now included on our consolidated statements of financial position. This significant amount of aggregate debt and the substantial amount of cash required for payments of interest and principal could adversely affect our liquidity. In particular, if we are unable to realize the anticipated benefits of the Shire Acquisition, we may not be able to service our indebtedness. We are also required to comply

with certain covenants within various financing arrangements and violations of such covenants may require the acceleration and immediate repayment of the indebtedness, which may in turn have a material adverse effect on our financial condition. Furthermore, we may desire to or be required from time to time to incur additional borrowings, including in relation to the repayment or refinancing any of our currently outstanding indebtedness. Our ability to arrange a re-financing will depend on our financial position and performance, prevailing market conditions and other factors beyond our control. Moreover, if we decide to refinance indebtedness as it comes due, our overall leverage may not necessarily decrease.

We have set goals to reduce the extent of leverage, and we are disposing certain non-core assets to generate cash in order to increase the pace of deleveraging. However, we may not be able to meet our goals if we are unable to sufficiently decrease our overall indebtedness, or if we are unable to achieve sufficient increases in earnings to offset our increased levels of debt. We may also not be successful in selecting non-core assets for disposal, and disposals may affect our business, financial condition or results of operations adversely, leading to larger-than-expected decreases in earnings. We may also not be able to dispose of such assets successfully in a manner that allows us to meet our goals or at all.

Credit rating agencies routinely evaluate our business, and their ratings are based on a number of factors, including our leverage, ability to generate cash flows, overall financial strength and diversification, as well as other factors beyond our control, such as the state of the global economy and our industry generally. For example, if we are unable to decrease our leverage, we may be unable to improve our credit ratings or be subject to ratings downgrades or other adverse actions by third-party ratings agencies. While our credit ratings remain investment grade, each rating agency reviews its ratings periodically, and there is no assurance that the current credit ratings assigned to us will not be downgraded. A downgrade of our credit ratings may materially and adversely affect the market prices of our equity and debt securities, the interest rates at which our borrowings are made and debt securities are issued, and fees charged to us by current or future lenders. This could make it significantly more costly for us to borrow money, to issue debt securities and to raise certain other types of capital and/or complete additional financings. Such negative credit ratings actions and the underlying reasons for such actions could materially and adversely affect our cash flows, results of operations and financial condition and the market price of, and our ability to pay the principal of and interest on, our debt securities.

Research and development of pharmaceutical products are expensive and subject to significant uncertainties, and we may be unsuccessful in bringing commercially successful products to market or recouping development costs.

Our ability to offset the effects of losses of exclusivity in our existing products and to continue to grow our business depends significantly on the success of our research and development activities in identifying, developing and successfully commercializing new products in a timely and cost-effective manner. To accomplish this, we commit substantial efforts, funds and other resources to research and development, both in-house and through collaborations with third parties. However, these research and development programs are expensive and involve intensive preclinical evaluation and clinical trials in connection with a highly complex and lengthy regulatory approval process. We discuss regulatory considerations below under “If we fail to comply with government regulations over product development, regulatory approvals and reimbursement requirements, our business could be adversely affected.” The research and development process for a new pharmaceutical product also requires us to attract and retain sufficient numbers of highly-skilled employees and can take up to 10 years to 15 years or longer from discovery to commercial launch. Moreover, even if we successfully develop and bring to market new products, there is only a limited available patent life in which to recoup these development costs.

During each stage of the approval process and post-approval life cycle of our products, there is a substantial risk that we will encounter serious obstacles, including the following:

- unfavorable results from preclinical testing of a new compound;
- difficulty in enrolling patients in clinical trials, or delays or clinical trial holds at clinical trial sites;
- delays in completing formulation and other testing and work necessary to support an application for regulatory approval;
- adverse reactions to the product candidate or indications of other safety concerns;
- insufficient clinical trial data to support the safety or efficacy of the product candidate;
- difficulty or delays in obtaining all necessary regulatory approvals in each jurisdiction where we propose to market such products;
- failure to bring a product to market prior to a competitor, or to develop a product sufficiently differentiated from a competing product to achieve significant market share;
- difficulty in obtaining reimbursement at satisfactory rates for our approved products from governments and insurers;
- difficulty in obtaining regulatory approval for additional indications;
- failure to enter into or implement successful alliances for the development and/or commercialization of products;
- inability to manufacture sufficient quantities of a product candidate for development or commercialization activities in a timely or cost-efficient manner; and
- the degree of market acceptance of any approved product candidate by the medical community, including physicians, healthcare professionals and patients, will depend on a number of factors, including relative convenience and ease of administration, the prevalence and severity of any adverse reactions, availability of alternative treatments, pricing and our sales and marketing strategy.

In addition, to the extent that new regulations raise the costs of obtaining and maintaining product authorizations or limit the economic value of a new product to its originator, our profitability and growth prospects could be diminished. Development of new and innovative products can also require the use of emerging platforms and technologies for which regulations either do not yet exist or are under development or modification. This may lead to greater uncertainty and risk in establishing the necessary data for approvals to conduct clinical trials and/or receiving marketing approvals.

As a result of the foregoing or other factors, we may decide to abandon the development of potential pipeline products in which we have invested significant resources, even where the product is in the late stages of development. Moreover, there can also be no assurance that we will be successful in bringing new products to market, marketing them, achieving sufficient acceptance thereof and recouping our investments in their development. For example, our pipeline compounds may not receive regulatory approval, become commercially successful or achieve satisfactory rates of reimbursement. Additionally, products approved for use and successfully marketed in one market may be unable to obtain regulatory approval, become

commercially successful or achieve satisfactory rates of reimbursement in other markets. As a result, we may be unable to earn returns on investments that we originally anticipated or at all, or may be forced to revise our research and development strategy, and our business, financial condition and results of operations could be materially and adversely affected.

If we fail to comply with government regulations over product development, regulatory approvals and reimbursement requirements, our business could be adversely affected.

Obtaining marketing approval for pharmaceutical products is a lengthy, complex and highly regulated process that requires intensive preclinical and clinical data, and the approval process can vary significantly depending on the regulatory authority. Relevant health authorities may, at the time of the filing of the application for a marketing authorization, or later during their review, impose requirements that can evolve over time, including requiring additional clinical trials, and such authorities may delay or refuse to grant approval. Even where we have obtained marketing approval for a product in one or more major markets, we may need to invest significant time and resources in applying for approval in other markets, and there is no assurance that we will be able to obtain such approval. In recent years, health authorities have become increasingly focused on product safety and on the risk/benefit profile of pharmaceutical products, which could lead to more burdensome and costly approval processes and negatively affect our ability to obtain regulatory approval for products under development. For example, the U.S. Food and Drug Administration (the "FDA"), the European Medicines Agency (the "EMA"), and the Pharmaceuticals and Medical Devices Agency (the "PMDA") in Japan have been implementing strict requirements for approval, particularly in terms of the volume of data needed to demonstrate a product's efficacy and safety.

Even after regulatory approval is obtained, marketed products are subject to various post-approval requirements, including continual review, risk evaluations, comparative effectiveness studies and, in some cases, requirements to conduct post-approval clinical trials to gather additional safety and other data. Regulatory authorities in many countries have worked to enhance post-approval monitoring in recent years, which has increased post-approval regulatory burdens. Post-regulatory approval reviews and data analyses can lead to the issuance of recommendations by government agencies, specialized organizations, health professionals or patients regarding the use of products. For example, such recommendations could include a request to limit the patient population of a drug's indication, the imposition of marketing restrictions, including changes in product labeling, or the suspension or withdrawal of the product. Any such recommendation, whether implemented or not, could result in reductions in sales volume and/or new or increased concerns about the adverse reactions or efficacy of a product. These substantial regulatory requirements have, over time, increased the costs associated with maintaining regulatory approvals and achieving reimbursement for our products.

If the regulatory approval process or post-approval, reimbursement, monitoring or other requirements become significantly more burdensome in any of our major markets, we could become subject to increased costs and may be unable to obtain or maintain approval to market our products. Any such adverse changes could materially and adversely affect our business, results of operations or financial condition.

If we fail to comply with laws and regulations governing the sales and marketing of our products, our business could be adversely affected.

We engage in various marketing, promotional and educational activities pertaining to, as well as the sale of, pharmaceutical products in a number of jurisdictions around the world. The promotion, marketing and sale of pharmaceutical products and medical devices is highly regulated and the sales and marketing practices of market participants such as us have been subject to increasing supervision by governmental authorities, and we believe that this trend will continue.

For example, in the U.S., our sales and marketing activities are monitored by a number of regulatory authorities and law enforcement agencies, including the U.S. Department of Health and Human Services (the "HHS"), the FDA, the U.S. Department of Justice, the U.S. Securities and Exchange Commission (the "SEC") and the Drug Enforcement Administration (the "DEA"). These authorities and agencies and their equivalents in other countries have broad authority to investigate market participants for potential violations of laws relating to the sale, marketing and promotion of pharmaceutical products and medical devices, including the False Claims Act, the Anti-Kickback Statute, the United Kingdom Bribery Act of 2010 and the Foreign Corrupt Practices Act, among others, for alleged improper conduct, including corrupt payments to government officials, improper payments to medical professionals, off-label marketing of pharmaceutical products and medical devices, and the submission of false claims for reimbursement by the federal government. Healthcare companies may also be subject to enforcement actions or prosecution for such improper conduct. Any inquiries or investigations into the operations of, or enforcement or other regulatory action against, us by such authorities could result in significant defense costs, fines, penalties and injunctive or administrative remedies, distract management to the detriment of the business, result in the exclusion of certain products, or us as a whole, from government reimbursement programs or subject us to regulatory controls or government monitoring of its activities in the future. We are also subject to certain ongoing investigations by governmental agencies.

Government policies and other pressures to reduce medical costs could have an adverse effect on sales of our pharmaceutical products.

We are subject to governmental regulations mandating price controls in various countries in which we operate. The growth of overall healthcare costs as a percentage of gross domestic product in many countries means that governments and payers are under intense pressure to control spending even more tightly. See Item 4. Information on the Company-B. Business Overview-Third Party Reimbursement and Pricing.

In the U.S., there has been increasing pricing pressure from managed care groups and institutional and governmental purchasers. In particular, as managed care groups have grown in size due to market consolidation, pharmaceutical companies have faced increased pressure in pricing and usage negotiations, and there is fierce competition among pharmaceutical companies to have their products included in the care providers' formularies. Moreover, as a result of the changing legislative and regulatory environment, including, for example, as a result of the upcoming 2020 presidential election, in the U.S. we have experienced heightened pricing pressure on, and limitations on access to, our branded pharmaceutical products sold in the U.S. There has

been increasing attention paid to the level of pricing of pharmaceutical products by policymakers and stakeholders, which could lead to political pressure or legislative, regulatory or other efforts to introduce lower prices, and change how the pharmaceutical supply chain could operate. In addition, there are efforts by the federal government to reduce spending on the Medicare and Medicaid programs, including proposals by the Congressional Budget Office to require pharmaceutical companies to pay a minimum rebate on drug products covered under Medicare Part D for low-income beneficiaries and to cap federal Medicaid payments to the states. Congressional proposals to convert the Medicare fee-for-service program into a premium support program could also lead to significant reductions in Medicare spending. The future of the U.S. healthcare legislation, as well as the potential impact of any new legislation, is uncertain, but we expect the health care industry in the U.S. will continue to be subject to increasing pricing and spending pressure, including from regulation and political and legal action.

In Japan, manufacturers of pharmaceutical products must have new products listed on the National Health Insurance (the "NHI") price list published by the Ministry of Health, Labour and Welfare of Japan (the "MHLW") for the coverage under the public medical care insurance systems. The NHI price list provides rates for calculating the price of pharmaceutical products used in medical services provided under various public medical care insurance systems. Prices on the NHI price list have been subject to revision generally once every two years on the basis of the actual prices at which the pharmaceutical products are purchased by medical institutions in Japan after discounts and rebates are deducted from the listed price. The average price of previously listed products generally decreases as a result of these price revisions. The Japanese government is currently undertaking healthcare reform initiatives with a goal of sustaining the universal coverage of the NHI program, and is addressing the efficient use of drugs, including promotion of generic use with a target of 80% penetration by volume by September 2020 with respect to products for which market exclusivity has expired. As part of these initiatives, the NHI price list is expected to be revised annually from April 1, 2021, which could lead to more frequent downward price revisions. In addition, cost-effectiveness analysis was officially introduced by the MHLW in April 2019. Products on the NHI price list nominated based on pre-defined criteria, such as the innovativeness and the financial impact, will be subject to review, and subject to price adjustments depending on outcome of this review.

In Europe, as in the U.S., drug prices have been subject to downward pressure due to measures implemented in each country to control drug costs, and prices continue to come under pressure due to parallel imports, generic competition, increasing use of health technology assessment based upon cost-effectiveness and other factors. European pricing and reimbursement authorities have also intensified efforts to increase transparency of prices as well as exchange of information among the various European pricing authorities in order to raise pressure towards the industry. This pricing debate has impacted the overall political climate in Europe and has triggered a European policy initiative to review the pharmaceutical industry's intellectual property incentives with a particular emphasis on orphan drugs. Any new legislation in this area would take at least two to three years to be adopted but could have significant impact on our business model. We are also facing similar pricing pressures in other regions, such as various emerging countries.

We are also facing similar pricing pressures in other regions and countries including China. We expect such pricing pressures to continue as we expand our business in those regions and countries.

We expect these efforts to control costs to continue as healthcare payers around the globe, in particular government-controlled health authorities, publicly funded or subsidized health programs, insurance companies and managed care organizations (the "MCOs"), increasingly pursue initiatives to reduce the overall cost of healthcare, restrict access to higher-priced new medicines, increase the use of generics and impose overall price revisions. Such further implementation of these policies could have a material adverse effect on our business, financial condition and results of operations.

The expiration or loss of patent or regulatory data protection over our products or patent infringement by generic manufacturers could lead to significant competition from generic versions of the relevant product and lead to declines in market share and price levels of our products.

Our pharmaceutical products are generally protected for a defined period by various patents (including those covering drug substance, drug product, approved indications, methods of administration, methods of manufacturing, formulations and dosages) and/or regulatory exclusivity, which are intended to provide us with exclusive rights to market the products for the life of the patent or duration of the regulatory data protection period. The loss of market exclusivity for pharmaceutical products opens such products to competition from generic substitutes that are typically priced significantly lower than the original products, which typically adversely affects the market share and prices of the original products.

Generic substitutes have high market shares in a number of key markets, including the U.S., Europe and many emerging countries, and the adverse effects of the launch of generic products are particularly significant in such markets. The introduction of generic versions of a pharmaceutical product typically leads to a swift and substantial decline in the sales of the original product. Our active life cycle management efforts cannot fully mitigate the impact of competition from generics. In the U.S. and the European Union ("EU"), for example, political pressure to reduce spending on prescription drugs has led to legislation and other measures that encourage the use of generic products. In Japan, the government is implementing various measures to control drug costs, including by encouraging medical practitioners to use and prescribe generic drugs, and in June 2017 announced its intention to raise generic drug penetration with respect to products for which market exclusivity has expired to 80% by volume by September 2020. Legislation has also been passed in the U.S. and Europe encouraging the use of biosimilar products. Similar to generics, biosimilars aim to provide less expensive versions of innovative biologic products. New legislation has provided abbreviated pathways for the approval and marketing of biosimilar products, which may affect the profitability and commercial viability of our biologic products.

Certain of our products have begun to, or are expected over the next several years to, face declining sales due to the loss of market exclusivity. For example, following the expiration of patent protection over bortezomib, the active ingredient in *VELCADE*, one of our largest selling products in the U.S., a competing bortezomib-containing product has been introduced. This has led to a decrease in sales of *VELCADE*, and further entry of competing products could result in substantial additional declines. Such decreases may accelerate following the scheduled expiration of patent protection over the formulation of *VELCADE* in 2022, or earlier if a competitor is able to develop a way to formulate *VELCADE* in a manner that does not infringe the relevant patent or succeed in getting the formulation patent invalidated. Patent protections over *VYVANSE*, which we acquired as part of the Shire

Acquisition and which was Shire's largest selling product, are scheduled to expire in 2023, which we anticipate will lead to declines in sales. *ENTYVIO*, which is currently our top selling product, will begin to lose regulatory exclusivity in the EU in 2024 and in the U.S. and Japan in 2026, and we expect to see decreased sales of *ENTYVIO* in the long term as a result.

We may also be subject to competition from generic drug manufacturers prior to the expiration of patents if a manufacturer successfully challenges the validity of our patents, or if the manufacturer believes that the benefits of launching the generic drug at risk (prior to the expiration of our patent) outweigh the costs of defending infringement litigation. For example, we received notice in June 2020 that an abbreviated new drug application (an "ANDA") to sell a generic version of *VYVANSE* was filed in the U.S. which could lead to a challenge to the relevant patents and the possibility of the introduction of a generic competitor prior to its scheduled expiration. If such a competitor launches a generic product at risk before the initiation or completion of court proceedings, a court may decline to grant us a preliminary injunction to halt further at risk sales and remove the infringing product from the market. While we may be entitled to obtain damages subsequently, the amount we may ultimately be awarded and able to collect may be insufficient to compensate for the loss of sales and other harm caused to us. Furthermore, if we lose patent protection as a result of an adverse court decision or a settlement, in certain jurisdictions, we may face the risk that government and private third-party payers and purchasers of pharmaceutical products may claim damages alleging they have over-reimbursed or overpaid for a drug.

If our patent and other intellectual property rights are infringed by generic drug manufacturers or other third parties, we may not be able to take full advantage of the potential or existing demand for our products. The protection that we are able to obtain for our prescription drugs varies from product to product and country to country and may not always be sufficient because of local variations in issued patents, or differences in national law or legal systems, including inconsistency in the enforcement or application of law and limitations on the availability of meaningful legal remedies. In particular, patent protection in emerging markets is often less certain than in developed markets. Certain countries may also engage in compulsory licensing of pharmaceutical intellectual property to other manufacturers as a result of local political pressure. Furthermore, the attention of our management and other personnel could be diverted from their normal business activities if we decide to litigate against such infringement. The realization of any such risks could adversely and materially affect our business, financial condition and results of operations.

We may have difficulty maintaining the competitiveness of our products.

The pharmaceutical industry is highly competitive, and in order to maintain the competitiveness of our product portfolio, we are required to maintain ongoing, extensive research for technological innovations, including new compounds, to develop and commercialize existing pipeline products, to expand our product portfolio through acquisitions and in-licensing, and to market our products effectively, including by communicating the efficacy, safety and value of our products to healthcare professionals. However, healthcare professionals and consumers may choose competitors' products over ours nonetheless, if they perceive these products to be safer, more reliable, more effective, easier to administer or less expensive. The success of any product depends on our ability to effectively communicate with and educate the healthcare professionals and patients and convince them of the advantage of our products over those of our competitors. We often carry out costly clinical trials even after our products have been launched to produce data to be utilized for these purposes, but such trials do not always produce the desired outcomes. Furthermore, many of our competitors have greater financial and other resources to conduct such trials in more detail and with larger patient populations, which may ultimately enable them to promote their products more effectively than we do. Moreover, if relevant regulators increase their approvals of new therapies developed by competitors for the conditions treated by our products, such as in order to increase the number of treatment options available for rare or orphan diseases, our business and results of operations could be materially and adversely affected.

For example, in recent years, competitors have introduced novel hemophilia products, or such products have been approved for additional uses, which may affect (and in certain cases has affected) sales of our recombinant and plasma-based hemophilia products, such as our factor FVIII products and *FEIBA*. Moreover, certain competitors are developing other hemophilia therapies, including gene-based therapies, which, if successfully introduced, could also affect sales of our recombinant and plasma-based therapies. Increased competition from new products or therapies could similarly affect our other products.

In Japan, reduced approval times for drugs already marketed outside Japan have led to increased competition through the introduction of such drugs into the Japanese market by foreign competitors. In addition, new competing products or the development of superior medical technologies and other treatment options could make our products or technologies lose their competitiveness or become obsolete. As discussed above, our products are also subject to competition from inexpensive generic versions of our products, as well as generic versions of our competitors' products, upon the expiration or loss of related patent protection and regulatory data protection, which may result in loss of market share. If we are unable to maintain the competitiveness of our products, our business, financial position and results of operations could be materially and adversely affected.

Furthermore, sales of the rare disease portfolio are particularly concentrated among small groups of customers, and we may be disproportionately affected by changes in their purchasing patterns, including if we are unable to maintain the competitiveness of our products.

We are subject to the risk of intellectual property infringement claims directed at us by third parties.

We are subject to the risk of infringement claims directed at us by third parties, even if we do not knowingly infringe on any valid third-party intellectual property rights. Although we monitor our operations to prevent infringement on the intellectual property rights of third parties, if we are found to have infringed the intellectual property rights of others or if we agree to settle infringement claims, we may be required to recall the relevant products, terminate manufacturing and sales of such products, pay significant damages or pay significant royalties.

We evaluate any such infringement claims to assess the likelihood of unfavorable outcomes and to estimate, if possible, the amount of potential losses. Based on these assessments and estimates, and in keeping with applicable accounting and disclosure standards, we establish reserves

and/or disclose the relevant litigation claims or decide not to establish reserves or disclose litigation claims. These assessments and estimates are based on the information available to our management at such time and involve a significant amount of management judgment. Actual outcomes or losses may differ materially from those envisioned by our current assessments and estimates. Although the parties to such patent and intellectual property disputes in the pharmaceutical industry have often settled through licensing or similar arrangements, the costs associated with these arrangements may be substantial and could include the payment of ongoing royalties. Furthermore, the necessary licenses may not be available on acceptable terms or at all. Therefore, if we are unable to successfully defend against infringement claims by third parties, our financial results could be materially and adversely affected.

We assumed certain tax related risks in connection with the Shire Acquisition, which could result in significant liability if the relevant tax authorities take a position that amounts received or transactions are taxable.

In connection with the Shire Acquisition, we assumed certain tax related risks related to the legacy Shire business, including the tax treatment of the break fee of 1.635 billion USD that Shire received in connection with the terminated offer to acquire Shire made by AbbVie, Inc. in 2014. In this respect, the Irish Revenue issued an assessment received by Shire on November 28, 2018 for 398 million EUR on the basis that the break fee was a taxable capital gain, which was contrary to the advice that Shire received. Based on continued advice that no tax liability should arise from the break fee, Shire appealed the assessment and the appeals process is continuing. However, the appeal may not be successful and at this time the outcome is unknown. In addition, in connection with its acquisition of Baxalta Incorporated ("Baxalta") in 2016, Shire agreed to indemnify Baxter International Inc., its affiliates and each of their respective officers, directors and employees against certain tax-related losses if the merger of Baxalta and Shire causes the prior spin-off of Baxalta by Baxter and related transactions to fail to qualify as tax-free. Although Shire received an opinion of tax counsel that the merger will not cause such prior transactions to fail to qualify as tax-free, such opinion is not binding on the tax authorities and the potential tax indemnification obligations are not limited in amount.

We may not be able to adequately expand our product portfolio through third-party alliance arrangements.

We expect that we will continue to rely on third parties for key aspects of our business, including the discovery and development of new products, in-licensing products, and the marketing and distribution of approved products. A major part of our research and development strategy is to initiate alliances with third parties in the biotechnology industry, academia and the public sector, and we believe that the overall strength of our research and development program and product pipeline depends on our ability to identify and initiate partnerships, in-licensing arrangements and other collaborations with third parties. However, there can be no assurance that any of our third-party alliances will lead to the successful development and marketing of new products. Moreover, reliance on third-party alliances subjects us to a number of risks, including:

- We may be unable to identify suitable opportunities at a reasonable cost and on terms that are acceptable to us due to active and intense competition among pharmaceutical groups for alliance opportunities or other factors;
- Entering into in-licensing or partnership agreements may require the payment of significant milestones well before the relevant products are placed in the market, without any assurance that such investments will ultimately become profitable in the long term. To the extent such milestone payments are recorded as assets on our consolidated statement of financial position, any termination of the relevant partnership could require us to recognize an impairment loss up to the full value of such asset;
- When we research and market our products through collaboration arrangements, the performance of certain key tasks or functions are the responsibility of our collaboration partners, who may not perform effectively or otherwise meet our expectations; and
- Decisions may be under the control of or subject to the approval of our collaboration partners, and we may have differing views or be unable to agree upon an appropriate course of action. Any conflicts or difficulties that we may have with our partners during the course of these agreements or at the time of their renewal or renegotiation or any disruption in the relationships with our partners may affect the development, launch and/or marketing of certain of our products or product candidates.

In addition, a licensor may attempt to terminate its license agreement with us or elect not to renew it to pursue other marketing opportunities. Our licensors also could merge with or be acquired by another company or experience financial or other setbacks unrelated to our licensing arrangements. Any of these events may force us to abandon a development project and adversely affect our ability to adequately expand or maintain our product portfolio.

The COVID-19 pandemic may negatively affect our business, operating results and financial condition, and has negatively affected the trading price of our common stock and ADSs.

In December 2019, a novel strain of coronavirus ("COVID-19") was reported to have originated in China. As COVID-19 continued to spread to other regions of the world, including, among others, Japan, North America, Europe and the U.K., the World Health Organization categorized the outbreak as a pandemic in March 2020. Global efforts to contain the spread of COVID-19 have continued to intensify in affected regions, with such efforts including travel restrictions, shelter-in-place orders and/or curfews, facility closures and the extended shutdown of businesses. We have taken a number of actions in response to the spread of COVID-19, including implementing remote work arrangements where possible, canceling non-essential business travel, decreasing in-person meetings between our sales representatives and prescribers and placing a general pause on the initiation of new studies, other than for the development of "CoVIg-19", a hyperimmune globulin treatment for COVID-19 being jointly developed with the other members of the CoVIg-19 Plasma Alliance, as well as new patient enrollment for ongoing studies with a small number of exceptions. The outbreak and preventative or protective actions that governments, corporations, individuals or we have taken or may take in the future to contain the spread of COVID-19 may result in a period of reduced operations, decreased product demand including due to reduced numbers of in-person meetings with prescribers, patient visits with physicians, vaccinations and elective surgeries, further delays in the start of clinical trials or other research and development efforts, business disruption for us and our suppliers, subcontractors, customers and other third parties

with which we do business and potential delays or disruptions related to regulatory approvals. However, these measures may not be effective in stopping or significantly slowing the spread of COVID-19 in general or at our facilities, and there may be multiple waves of outbreaks. The effects of the outbreak and related actions, including if significant portions of our workforce are unable to work effectively due to facility closures, issues relating to productivity or data security arising from the implementation of remote working arrangements, illness, quarantines, government actions, our actions, like those mentioned above, or other restrictions, may therefore hinder or delay our production capabilities (and, in particular, have resulted in a temporary decline in our plasma collections) and otherwise impede our ability to perform on our obligations to our customers, and may also result in increased costs to us. The outbreak and related actions may also prevent our suppliers, vendors or subcontractors from meeting their obligations to us, including the supply of plasma, which has no substitute, which could also impair our ability to meet our supply obligations or execute our business plans in a timely manner or at all, or require us to incur significant additional costs. Any costs associated with the COVID-19 outbreak may not be fully recoverable or adequately covered by insurance. The outbreak and related actions may also result in reduced customer demand or limit the ability of customers, including governments or government agencies, to perform their obligations to us, including in making timely payments to us. Any of these factors, depending on the severity and duration of the outbreak and its effects, could have a material adverse effect on our business, results of operations and financial condition.

The financial impact of these factors cannot be reasonably estimated at this time but may materially affect our business, financial condition and results of operations, and the trading prices of our common stock and ADSs were impacted by volatility in the financial markets resulting from the pandemic. The full extent to which the pandemic impacts our business, results or the trading price of our common stock and ADSs will depend on future developments, which are highly uncertain and cannot be predicted, including new information which may emerge concerning the severity and duration of the pandemic and actions to contain its spread or treat its impact, among others.

We have significant operations across the world, including emerging markets, which expose us to additional risks.

Our global operations, which encompass approximately 80 countries and regions across the world, are subject to a number of risks, including the following:

- difficulties in monitoring and coordinating research and development, marketing, supply-chain and other operations in a large number of jurisdictions;
- risks related to various laws, regulations and policies, including those implemented following changes in political leadership and trade, capital and exchange controls;
- changes with respect to taxation, including impositions or increases of withholding and other taxes on remittances and other payments by our overseas subsidiaries;
- varying standards and practices in the legal, regulatory and business cultures in which we operate, including potential inability to enforce contracts or intellectual property rights;
- trade restrictions and changes in tariffs;
- complex sanctions regimes in various countries such as the U.S., the EU and other jurisdictions, violations of which could lead to fines or other penalties;
- risks related to political instability and uncertain business environments;
- changes in the political, economic or social climate, including inter-country relationships;
- acts of terrorism, war, global climate change, extreme weather events, medical epidemics or pandemics such as the recent COVID-19 pandemic, and other sources of social disruption; and
- difficulties associated with managing local personnel and preventing misconduct by local third-party alliance partners.

Any one or more of these or other factors could increase our costs, reduce our revenues, or disrupt our operations, with possible material adverse effects on our business, financial condition and results of operations. Further expansion overseas has been one of our key strategies, and, in the fiscal year ended March 31, 2020, regions outside of Japan accounted for 82.0% of our consolidated revenue, with the U.S. in particular contributing 48.5% of consolidated revenue. We expect that markets outside Japan, particularly the U.S. and also Europe, the U.K., Canada and emerging markets, will continue to be increasingly important to our business and results of operations, increasing the likelihood that any of these risks is realized. We have been also taking steps to grow our business in emerging markets, which we define to include Russia/Commonwealth of Independent States (“CIS”), Latin America, Asia (excluding Japan) and Other (including the Middle East, Oceania and Africa). Our revenue from emerging markets was 456.9 billion JPY (or 13.9% of our total revenue) for the fiscal year ended March 31, 2020, and we intend to pursue further growth in such emerging markets. In particular, we believe that there is an attractive opportunity to grow our business in China.

However, there is no guarantee that our efforts to expand sales in emerging markets will succeed. Some countries may be especially vulnerable to periods of global financial instability or may have very limited resources to spend on healthcare. Emerging markets present particular challenges in obtaining funding, achieving market access for our products and successfully ensuring that we receive appropriate levels of reimbursement. Emerging markets also tend to require substantial efforts in patient support and other programs. All of these factors may adversely affect the profitability of our businesses in these emerging markets.

In order to successfully implement our emerging markets strategy, we must also attract and retain qualified personnel, despite the possibility that some emerging markets may have a relatively limited number of persons with the required skills and training. We may also be required to increase our reliance on third-party agents within less-developed markets, which may put us at increased risk of liability. In addition, many emerging markets have currencies that fluctuate substantially, and if such currencies are devalued and we cannot offset the devaluations, our financial performance in such countries may be adversely affected. Further, many emerging markets have relatively weak intellectual property protection and inadequate protection against crime, including counterfeiting, corruption and fraud. Operations in certain emerging countries, where corruption may be more prevalent than in more developed countries and where internal compliance practices may not be well established, may also pose challenges from a legal and regulatory compliance perspective. Moreover, we may face additional legal and regulatory barriers to achieving growth, such as restrictions on the import of raw

materials or other trade regulations (for example, on the import of plasma into China) that will require us to expend additional resources to achieve our goals.

For reasons including but not limited to the above, significant parts of our operations across the world including emerging markets presents significant risks, and the realization of such risks could have a material adverse effect on our business, financial condition and results of operations.

We face risks relating to the exit of the United Kingdom from the European Union.

The U.K.'s withdrawal from the EU (commonly known as "Brexit") became effective on January 31, 2020. The subsequent transition period (sometimes called the implementation period) is expected to last until December 31, 2020 and creates uncertainties affecting business operations in the EU. The withdrawal by the U.K. from the EU, particularly if the transition period expires without a trade agreement between the U.K. and the EU, could result in the deterioration of economic conditions, volatility in currency exchange rates, and increased regulatory complexities, as well as the potential for product shortages, increased costs or other similar effects. Given the lack of progress on a future trade agreement between both parties, regulatory arrangements for the U.K. beyond December 2020 have not been clarified, which could impact our future operations in the U.K. Particular uncertainty exists about the most appropriate way to supply medicines to Northern Ireland after December 31, 2020, given the lack of agreement on how the Northern Ireland Protocol will be implemented with regard to medicines.

The potential impact of Brexit on our market share, sales, profitability and results of operations is unclear. Depending on these outcomes during and after the transition period, as well as any potential impact on the EMA, economic conditions in the U.K., the EU and global markets may be adversely affected by reduced growth and volatility. Such volatility and negative economic impact could, in turn, adversely affect our revenues, financial condition or results of operations.

Our results of operations and financial condition may be adversely affected by foreign currency exchange rate fluctuations.

We manufacture and sell products to customers in numerous countries, and we have entered and will enter into acquisition, licensing, borrowings or other financial transactions that give rise to translation and transaction risks related to foreign currency exposure. Fluctuations in currency exchange rates in the markets where we are active could negatively affect our results of operations, financial position and cash flows. For the fiscal year ended March 31, 2020, 82.0% of our sales were in markets outside Japan. Our consolidated financial statements are presented in Japanese yen, and by translating the foreign currency financial statements of our foreign subsidiaries into yen, the amounts of our revenue, operating profit, assets and equity, on a consolidated basis, are affected by prevailing rates of exchange.

We utilize certain hedging measures with respect to some of our foreign currency transactions. However, such hedging measures do not cover all of our exposures and, even to the extent they do, they may only delay, or may otherwise be unable to completely eliminate, the impact of fluctuations in foreign currency exchange rates.

Our reliance on third parties for the performance of certain key business functions, particularly product manufacture and commercialization, heightens the risks faced by our business.

We rely on suppliers, vendors and partners, including alliances with other pharmaceutical companies, for certain key aspects of our business, including manufacture and commercialization of products, support for information technology systems and certain human resource functions. We do not control these partners, but we depend on them in ways that may be significant to us. If these parties fail to meet our expectations or fulfill their obligations to us, we may fail to receive the expected benefits. In addition, if any of these third parties fails to comply with applicable laws and regulations in the course of its performance of services for us, there is a risk that we may be held responsible for such violations as well. This risk is particularly serious in emerging markets, where corruption is often prevalent and where many of the third parties on which we rely do not have internal compliance resources comparable to our own. Any such failures by third parties, in emerging markets or elsewhere, could adversely affect our business, reputation, financial condition or results of operations.

Our dependence on third parties for the inputs for our products subjects us to various risks, and changes in the costs of materials may adversely affect our profitability.

Although we develop and manufacture the active ingredients used in some of our products at our own facilities, we are dependent on third-party suppliers for a substantial portion of the raw materials and compounds used in the products we produce. The price and availability of the raw materials for our products, including chemical compounds and biologics, are subject to the effects of weather, natural disasters, market forces, the economic environment, fuel costs and foreign exchange rates. If our cost for such materials increases, we may not be able to make corresponding increases in the prices of our products due to market conditions or our relationships with our customers, and as a result, our profitability could be materially and adversely affected.

In particular, we rely on third-party suppliers of key manufacturing inputs of certain drug products, including, but not limited to, *ADCETRIS, ADVATE*, *ADYNOVATE*, *ALUNBRIG, CINRYZE*, *CUVITRU*, *ENTYVIO, FEIBA*, *FIRAZYR*, *GATTEX/REVESTIVE*, *HYQVIA*, *LEUPRON, MEPACT, NINLARO, TAKHZYRO,* and *VELCADE*. Furthermore, certain active ingredients for these products are sourced from a single supplier. We also rely in part on third-party sources to provide the donated plasma necessary for our plasma-derived therapies. In addition, although we dual-source certain key products and/or active ingredients, we currently rely on a single source for production of the final drug product for certain of our products, including, but not limited to, *ADDERALL XR*, *ADYNOVATE*, *ALOFISEL, ALUNBRIG, CINRYZE*, *CUVITRU*, *FIRAZYR*, *HYQVIA*, *LIALDA, MEPACT, NINLARO,*

PENTASA and *TAKHZYRO*. Sources of some materials may be limited to a single supplier, and if such supplier faces any difficulty in supplying the materials, we may not be able to find an alternative supplier in a timely manner or at all. If materials become unavailable or if quality problems related to the materials arise, we may be forced to halt production and sales of products that use them. In the event that any of our third-party suppliers is delayed in its delivery of such raw materials or compounds, is unable to deliver the full quantity ordered by us at the appropriate level of quality, or is unable to deliver any raw materials or compounds at all, our ability to sell our products in the quantities demanded by the market may be impaired, which could damage our reputation and relationships with customers and patients. In such a case, our business and results of operations could be adversely affected.

The manufacture of our products is technically complex and highly regulated, and supply interruptions, product recalls or other production problems caused by unforeseen events may reduce sales, adversely affect our operating results and financial condition and delay the launch of new products.

The manufacture of our products is technically complex and highly regulated, and as a result we may experience difficulties or delays including but not limited to the following:

- seizure or recalls of products or shut-downs of manufacturing plants;
- problems with business continuity, including as a result of a natural or man-made disaster, at one of our facilities or at a critical supplier or vendor;
- failure by us or by any of our vendors or suppliers to comply with the Good Manufacturing Practice (the "GMP") and other applicable regulations and quality assurance guidelines, which could lead to manufacturing shutdowns, product shortages, delays in product manufacturing and /or administrative, enforcement or other actions by regulatory authorities if regulatory authorities deem our products to be adulterated or otherwise in violation of applicable laws;
- problems with manufacturing, quality assurance/quality control or supply, or governmental approval delays, due to our consolidation and rationalization of manufacturing facilities and the sale or closure of certain sites;
- failure of a sole source or single source supplier to provide us with necessary raw materials, supplies or finished goods for an extended period of time, which could impact continuous supply;
- failure of a third-party manufacturer to supply us with semi-finished or finished products on time;
- construction or regulatory approval delays related to new facilities or the expansion of existing facilities;
- the inability to obtain sufficient components or raw materials on a timely basis or at a cost-effective price due to public health crises, medical epidemics or pandemics such as the COVID-19 pandemic;
- additional costs related to deficiencies identified by regulatory agencies in connection with inspections of our facilities, and enforcement, remedial or punitive actions by regulatory authorities if we fail to remedy any deficiencies; and
- other manufacturing or distribution problems including limits to manufacturing capacity due to regulatory requirements (e.g. Registration, Evaluation, Authorisation and Restriction of Chemicals ("REACH") regulation in the EU), changes in the types of products produced, physical limitations or other business interruptions that could impact continuous supply.

In addition, despite efforts at compliance, from time to time we or our partners may receive notices of manufacturing, quality-related, or other observations following inspections by regulatory authorities around the world, as well as official agency correspondence regarding compliance. For example, on June 9, 2020 the FDA issued a warning letter related to our manufacturing plant in Hikari, Yamaguchi, Japan which included several technical observations, including observations about procedures, personnel, records, investigations, training, equipment, and oversight. We are reviewing the warning letter and will respond to the FDA within the required timeframe. This action resulted from a routine inspection by the FDA of our Hikari manufacturing plant in November 2019. Following the inspection, we immediately put into place a comprehensive corrective action/preventative action plan, and the issues raised as part of the inspection are being addressed within the context of those activities. However, we or our partners may receive additional or similar observations and correspondence in the future, whether regarding the Hikari plant or otherwise. If we are unable to resolve these observations and address regulator concerns in a timely fashion, our business, financial condition and results of operations could be materially affected.

The development and manufacture of biologics and stem cell therapies present heightened or additional risks. The manufacture of biologics, including stem cell products, is highly complex and is characterized by inherent risks and challenges, such as raw material inconsistencies, logistical and sourcing challenges, significant quality control and assurance requirements, manufacturing complexity (including heightened regulatory requirements) and significant manual processing. Unlike products that rely on chemicals for efficacy, such as most pharmaceuticals, biologics are difficult to characterize due to the inherent variability of biological input materials. As a result, assays of the finished product may not be sufficient to ensure that the product will perform in the intended manner. Problems with the manufacturing process, even minor deviations from the normal process, could result in product defects or manufacturing failures that result in, among other things, lot failures, product recalls, product liability claims or insufficient inventory, which could be costly to us or result in reputational damage.

Furthermore, sourcing and transportation of plasma and production and distribution of plasma-derived products is complex, capital intensive and subject to extensive regulation. If we are unable to manage these inherent risks and challenges, we may lose market share or customer confidence, be required to record charges related to idle capacity or impairment on facilities or take other actions which could materially and adversely affect the Plasma-Derived Therapies business.

Any of the above may reduce sales, delay the launch of new products, and adversely affect our business, financial condition and results of operations.

The illegal distribution and sale by third parties of counterfeit versions of our products or products stolen from us could have an adverse effect on our reputation and business.

Third parties may illegally distribute and sell counterfeit versions of our products, which do not meet the rigorous manufacturing and testing standards to which our products are subject. A patient who receives a counterfeit drug may be at risk for a number of dangerous health consequences. Reports of adverse reactions to counterfeit drugs or increased levels of counterfeiting could materially affect patient confidence in our products, which could have a material adverse effect on our reputation and financial results. In addition, thefts at warehouses, at plants, or in transit of inventory that is not properly stored or that is sold through unauthorized channels could materially and adversely affect patient safety, our reputation and our results of operations.

We are involved in litigation relating to our operations on an ongoing basis, and such litigation could result in financial losses or harm our business.

We are involved in various litigation relating to our operations on an ongoing basis, including claims related to product liability and intellectual property as well as to antitrust, sales and marketing and other regulatory regimes. Given the inherent unpredictability of litigation, it is possible that an adverse outcome in one or more pending or future litigation matters could have a material adverse effect on our operating results or cash flows. For a description of certain ongoing litigation, see Note 32 to our audited consolidated financial statements.

Economic, financial and environment conditions may have a material adverse effect on our business, financial condition and results of operations.

Growth of the global pharmaceutical market has become increasingly tied to global economic growth. In this context, a substantial and lasting slowdown of the global economy or major national economies could negatively affect growth in the global pharmaceutical market and, as a result, adversely affect our business. In particular, weak economic conditions can have a particularly adverse impact on pharmaceutical demand in markets having significant co-pays or lacking a developed third-party payer system, as individual patients may delay or decrease out-of-pocket healthcare expenditures. Negative economic developments could also reduce the sources of funding for national social security systems, leading to heightened pressure on drug prices, increased substitution of generic drugs, and the exclusion of certain products from formularies.

Following the global financial crisis in 2008, economic growth continued to be stagnant in major developed countries while the pace of growth in many emerging economies continued to decline. Since the outbreak of COVID-19, economic growth has and is expected to continue to significantly slow down. The U.K.’s exit from the EU, political volatility in the U.S., including in relation to the 2020 presidential election, continued instability in the Middle East and North Korea and global developments in trade and security policy have increased political and economic uncertainty. To the extent that economic or financial conditions continue to weaken and not improve in any of our major operating markets, demand for our products or product pricing could be negatively affected. In addition, to the extent that the current or future economic and financial conditions negatively affect the global business environment, we could experience a disruption or delay in the performance of third parties on which we rely for parts of our business, including collaboration partners and suppliers. See *“The COVID-19 pandemic may negatively affect our business, operating results and financial condition, and has negatively affected the trading price of our common stock and ADSs.”*

Such disruptions or delays could have a material and adverse effect on our business, financial condition and results of operations.

Our products may have unanticipated adverse effects or possible adverse effects, which may restrict use of the product or give rise to product liability claims.

As a pharmaceutical company, we are subject to significant risks related to product liability. Unanticipated adverse reactions or unfavorable publicity from complaints concerning any of our products, or those of our competitors, could have an adverse effect on our ability to obtain or maintain regulatory approvals or successfully market our products, and may even result in recalls, withdrawal of regulatory approval or adverse labeling of the product.

While our products are subject to comprehensive clinical trials and rigorous statistical analysis during the development process prior to approval, there are inherent limitations with regard to the design of such trials, including the limited number of patients enrolled in such trials, the limited time used to measure the efficacy of the product and the limited ability to perform long-term monitoring. In the event that such unanticipated adverse reactions are discovered, we may be required to add descriptions of the adverse reactions as precautions to the packaging of our products, recall and terminate sales of products or conduct costly post-launch clinical trials. Furthermore, concerns relating to potential adverse reactions could arise among consumers or medical professionals, and such concerns, whether justified or not, could have an adverse effect on sales of our products and our reputation. We could also be subject to product liability litigation by patients who have suffered or claim to have suffered such adverse reactions resulting in harm to their health.

Although we maintain product liability insurance at coverage levels that we believe are appropriate, we could be subject to product liability that significantly exceeds such levels. Product liability coverage is also increasingly difficult and costly to obtain, and may not be available in the future on acceptable terms. Therefore, in the future, it is possible that we may need to rely increasingly on self-insurance for the management of product liability risk. In cases where we self-insure, the legal costs that we would bear for handling such claims and potential indemnifications to be paid to claimants could materially and adversely affect our financial condition. In addition, the negative publicity from product liability claims, whether justified, may damage our reputation and may negatively impact the number of prescriptions of the product in question or our other products. As a result, our business, financial condition and results of operations could be materially and adversely affected.

Sales to wholesalers are concentrated, which exposes us to credit risks and pricing pressures.

A significant portion of our global sales are made to a relatively small number of wholesale distributors, retail chains and other purchasing groups. In the fiscal year ended March 31, 2020, there were two wholesale distributors, AmerisourceBergen Corporation and McKesson Corporation, that accounted for over ten percent of Takeda's total revenue. If one of our significant wholesale distributors encounters financial or other difficulties, such distributor may decrease the amount of business that it does with us, and we may be unable to collect the amounts that the distributor owes us on a timely basis or at all. Furthermore, the concentration of wholesale distributors has been increasing through mergers and acquisitions. In addition to increased credit risks, this has resulted in such distributors gaining additional purchasing leverage, which may increase pricing pressure on our products. Such credit concentration risks and pricing pressure could adversely affect our business, financial condition and results of operations.

We may not be able to attract and retain key management and other personnel.

In order to produce, develop, support and market our products, we depend on the expertise and leadership of our senior management team and other key members of our organization. The loss of key members of our organization, including senior members of our scientific and management teams, high-quality researchers and development specialists, could delay or prevent the achievement of major business objectives. The market for such talent has become increasingly competitive, including in specific geographic regions and in specialized fields such as clinical development and biosciences, and we are required to invest heavily in the recruitment, training and retention of qualified individuals, including salary and other compensation to reward performance and incentivize employees. Despite our efforts to retain them, key employees could terminate their employment with us for any reason or for no reason, and there is no assurance that we will be able to attract or retain key employees and successfully manage them. Our inability to attract, integrate and retain highly skilled personnel, particularly those in leadership positions, may weaken our succession plans and may materially adversely affect our ability to implement our strategy and meet our strategic objectives, which could ultimately adversely affect our business and results of operations.

We are increasingly dependent on information technology systems and our systems and infrastructure face the risk of theft, exposure, tampering or other intrusions.

A variety of important processes relating to the research and development, production and sale of our products depend heavily on our information systems, including cloud-based computing, or those of third party providers to whom we outsource certain business functions, including the storage and transfer of critical, confidential, sensitive or personal information regarding our patients, clinical trial subjects, vendors, customers, employees and others. We also increasingly seek to develop and collaborate on technology-based digital health products, such as mobile applications that aim to improve patient welfare in a variety of ways, which could lead us to store and transfer personal information about individual patients, customers and others. The size, age and complexity of our information technology systems make them potentially vulnerable to service interruptions, malicious intrusions and random attacks. Cyber-attacks are increasing in frequency, sophistication and intensity, and opportunistically in response to, for example, the spread of COVID-19 and implementation of remote working arrangements. These and other cyber-attacks are made by groups and individuals with a wide range of motives (including, but not limited to, industrial espionage) and expertise, including organized criminal groups, hacktivists, nation-states and others. Cyber-attacks could include the deployment of harmful malware, denial of service attacks, worms, social engineering and other means to affect service reliability and threaten data confidentiality, integrity and availability. The development and maintenance of systems to safeguard against such attacks is costly and requires ongoing monitoring and updating as technologies change and efforts to overcome security measures become increasingly more sophisticated. Moreover, the costs related to these security measures are expected to continue to increase. Despite our efforts, the possibility of a future data compromise cannot be eliminated entirely, and risks associated with intrusion, exposure, tampering, and theft remain. For zero-day threats, or new vectors of attack which are currently unknown, the risk that our defenses will be inadequate are particularly pronounced.

Although we have not, to date, detected any material breaches of our information technology systems, data systems or personal information, the risk of such breaches remains and cannot be completely negated. If our data systems are compromised, our business operations may be impaired, we may lose profitable opportunities, or the value of those opportunities may be diminished, and we may lose revenue because of unlicensed use of our intellectual property or confidential or proprietary information. Cyber-attacks could significantly impact the availability of data systems that are essential to conducting routine business operations across the company, including product manufacturing or clinical development, and the recovery efforts could be both time consuming and costly. If personal information of our customers or employees is misappropriated, our reputation with our customers and employees may be injured resulting in loss of business and/or morale, and we may incur costs to remediate possible injury to our customers and employees or be required to pay fines or take other action with respect to judicial or regulatory actions arising out of such incidents. Data privacy or security breaches by employees and others with permitted access to our systems, including in some cases third-party service providers to which we may outsource certain business functions, may also pose a risk that sensitive data, including intellectual property or personal information, will be exposed to unauthorized persons or to the public.

Changes in data privacy and protection laws and regulations, particularly in Europe, or any failure to comply with such laws and regulations, could adversely affect our business and financial results.

We are subject to laws and regulations globally regarding privacy, data protection, and data security, including those related to the collection, storage, handling, use, disclosure, transfer, and security of personal data. Significant uncertainty exists as privacy and data protection laws may be interpreted and applied differently from country to country and may create inconsistent or conflicting requirements. For example, the EU's General Data Protection Regulation (the "GDPR"), which imposes additional obligations on companies regarding the handling of personal data and provides certain individual privacy rights to persons whose data is processed, became effective on May 25, 2018. Moreover, significant regulatory fines may be imposed on us for violation of these requirements, particularly in the case of the GDPR, which are set at a maximum of the higher of 20 million EUR or 4% of

annual global turnover for the most serious breaches, or the higher of 10 million EUR or 2% of annual global turnover for certain others. There is also significant uncertainty as to how the various EU member states or individual regulators will implement and interpret the GDPR, and we are still in the process of identifying and unifying differences between our and Shire's historical GDPR compliance practices. Furthermore, legislators and regulators in the U.S. are proposing new and more robust cybersecurity rules in light of the recent broad-based cyber-attacks at a number of companies, as well as data privacy laws, such as the California Consumer Privacy Act, which became effective on January 1, 2020. Compliance with existing, proposed and recently enacted laws (including implementation of the privacy and process enhancements called for under GDPR) and regulations can be costly; any failure to comply with these regulatory standards could subject us to legal and reputational risks. Misuse of or failure to secure personal information could also result in violation of data privacy laws and regulations, proceedings against us by governmental entities or others or damage to our reputation and credibility and could also have a negative impact on revenues and profits.

Social media platforms and new technologies present risks and challenges for our reputation and business.

Consumers, the media, pharmaceutical companies and other parties increasingly use social media and other new technologies to communicate about pharmaceutical products and the diseases they are intended to treat. For pharmaceutical companies, the use of these technologies requires specific attention, monitoring programs and moderation of comments. For example, negative or inaccurate posts or comments about us or our products on any social media networking platforms could damage our reputation and business. Social media could also be used to bring negative attention to us or to the pharmaceutical industry as a whole, which could in turn cause reputational harm to us and negatively impact our business. The nature of evidence-based health care, however, may prevent us from rapidly and adequately defending our interests against such comments. In addition, our employees and partners may use social media and mobile technologies inappropriately, which may expose us to liability, or which could lead to breaches of data security, loss of trade secrets or other intellectual property or public disclosure of sensitive information, including information about our employees, clinical trial subjects or customers.

We face risks from the pursuit of acquisitions, and the anticipated benefits and synergies resulting from acquisitions may not be realized.

We regularly pursue acquisitions for several reasons, including strengthening our pipeline, complementing existing lines of business, adding research and development capabilities or pursuing other synergies. The pursuit of these acquisitions requires the commitment of significant management and capital resources in various stages, from the exploration of potential acquisition targets to the negotiation and execution of an acquisition to the integration of an acquired business into our own. The required commitment of time and resources may divert the attention of management or capital or other resources away from our day-to-day business. Moreover, we may not be able to recoup the investment of capital or other resources through the successful integration of acquired businesses, including the realization of any expected cost or other synergies. Specifically, we may encounter the following difficulties:

- We may face significant challenges in combining the infrastructure, management and information systems of acquired companies with ours, including integrating research and development, manufacturing, distribution, marketing and promotion activities and information technology systems;
- There may be difficulties in conforming standards, controls, procedures and accounting and other policies, as well as business cultures and compensation structures;
- We may not be able to retain key personnel at acquired companies, or our own employees may be motivated to leave due to acquisitions;
- We may not be successful in identifying and eliminating redundancies and achieving other cost savings as expected; and
- We may not be able to successfully realize benefits from acquired products, including pipeline products under development.

Integrating the operations of multiple new businesses with that of our own is a complex process that requires significant management attention and resources. The integration process may disrupt our existing and other newly acquired businesses and, if implemented ineffectively, could have an adverse impact not only on our ability to realize the benefits of a given acquisition but also on the results of our existing operations. Integration-related risks may be heightened in cases where acquired businesses' operations, employees or customers are located outside our major markets and we incur higher costs than anticipated due to regulatory changes, environmental factors or foreign exchange fluctuations. We continue to pursue strategic business acquisitions globally as a key part of our continuous growth strategy. If we are not able to achieve the anticipated benefits of any future acquisitions in full or in a timely manner, we could be required to recognize impairment losses, we may not be able to recoup our investment, and our business, financial position and results of operations could be materially and adversely affected. Particularly, we may be unable to achieve the expected revenues pursuant to licensing, co-promotion or co-development agreements or collaborations. We may also assume unexpected contingent or other liabilities, or be required to mark up the fair value of liabilities (or mark down the fair value of assets) acquired upon the close of an acquisition.

We may incur substantial costs due to our environmental compliance efforts or claims relating to our use, manufacture, handling, storage or disposal of hazardous materials.

Our research and development and manufacturing processes use hazardous materials, including chemicals and radioactive and biological materials, and produce hazardous waste. National and local laws and regulations in many of the jurisdictions in which we operate impose substantial potential liability for the improper use, manufacture, handling, storage and disposal of hazardous materials as well as for land contamination, and, in some cases, this liability may continue over long periods of time. Despite our compliance efforts, we cannot eliminate the risk of accidental contamination and any resultant injury from these materials. For example, real properties that we owned or used in the past or that we own or use now or in the future may contain detected or undetected contamination resulting from our manufacturing operations at those sites or the activities of prior owners or occupants. We may suffer from expenses, claims or liability which may fall outside of or exceed our insurance coverage. Furthermore, changes to current environmental laws and regulations may impose further compliance requirements on us that may impair our research, development and production efforts as well as our other business activities.

Our business may be adversely affected by climate change, extreme weather events, earthquakes, civil or political unrest, terrorism or other catastrophic events.

In recent years, extreme weather events and changing weather patterns such as storms, flooding, droughts and temperature changes have become more common. As a result, we are potentially exposed to various natural disasters or extreme weather risks such as hurricanes, tornadoes, droughts or floods, typhoons, tidal waves, wildfires or other events that may result from the impact of climate change on the environment. In addition, Japan, the U.S. and other regions in the world in which we operate are subject to the risk of natural disasters such as earthquakes, tsunamis and/or volcanic eruptions. Other events outside our control, such as war, civil or political unrest, deliberate acts of sabotage, terrorism or industrial accidents such as fire and explosion, whether due to human or equipment error, could damage, cause operational interruptions, or otherwise adversely affect certain of our manufacturing or other facilities as well as potentially cause injury or death to our personnel. In the event of a major natural disaster or other uncontrollable event or accident, our facilities, particularly our production plants, may experience catastrophic loss, operations at such facilities may be halted, shipments of products may be suspended or delayed and large losses and expenses to repair or replace facilities may be incurred. Such negative consequences could cause product shortages, significant losses of sales or require significant unexpected expenditures, and materially adversely affect our business, financial condition and results of operations. In addition, our business may also be adversely affected if our suppliers or business partners were to experience a catastrophic loss due to natural disasters, terrorism, accidents or other uncontrollable events.

Although we purchase comprehensive global insurance to cover property damage and consequent business interruption for certain potential losses at sites owned by us and at certain critical supplier sites, we do not maintain insurance policies to cover all potential losses and therefore our insurance policies may not be adequate to cover all possible losses and expenses. For instance, we do not maintain earthquake insurance in Japan.

We may experience difficulty implementing sustainability-related measures or in meeting the expectations of stakeholders.

In recent years, governmental and regulatory authorities, counterparties such as vendors and suppliers, investors, the public at large and others have increasingly focused on sustainability and social responsibility-related issues, particularly as they relate to the environment. Moreover, we have committed to reducing our carbon footprint, decreasing the waste created by our business and enhancing our water stewardship, and expect our vendors and suppliers to cooperate in these initiatives. However, we may be unable to meet such standards or achieve our goals, and our efforts to do so may for example impose significant additional costs on us, require us to seek alternative vendors or suppliers or impair our ability to procure or use certain materials. Conversely, if we are unable to meet such standards, we may not be able to continue to administer our business as we desire. Moreover, to the extent that we are unable to meet the expectations of stakeholders, including governmental and regulatory authorities, counterparties, investors, or the public, our reputation may be harmed, we may face increased compliance or other costs and demand for our securities and our ability to participate in the debt and equity markets may decrease. Furthermore, such standards and expectations are subject to ongoing change and refinement, and may shift in unexpected and potentially significant ways, which we may struggle to accommodate.

We may have to recognize additional charges on our statements of profit or loss due to impairment of goodwill, other intangible assets and equity method investments.

We carry significant amounts of goodwill and intangible assets on our consolidated statements of financial position as a result of past acquisitions, including the Shire Acquisition. As of March 31, 2020, we had goodwill of 4,012.5 billion JPY and intangible assets of 4,171.4 billion JPY. Goodwill and intangible assets recorded in relation to acquisitions are recognized on our consolidated statements of financial position on the acquisition date. Under IFRS, we are required to examine such assets for impairment annually or whenever events or changes in circumstances indicate that the carrying amount of an asset may not be recoverable. See Item 5. Operating and Financial Review and Prospects-A. Operating Results-Critical Accounting Policies-Impairment of Goodwill and Intangible Assets.

We occasionally enter into business ventures with third-party entities where we have significant influence over the decisions on financial and operating policies, but do not have control or joint control (referred to as investments in associates). We also enter into joint arrangements whereby we and the other parties that have joint control of the arrangement have rights to the net assets of the arrangement (referred to as joint venture). We account for these investments using the equity method of accounting. As of March 31, 2020, the carrying amount of investments accounted for using the equity method was 107.3 billion JPY. Under IFRS, at each reporting period, we are required to determine whether there is objective evidence that the investment in each associate or joint venture is impaired.

The recognition of such impairment charges may adversely affect our business, financial condition and results of operations.

If we fail to maintain effective internal control over financial reporting, the accuracy and timeliness of our financial reporting may be adversely affected, which could cause investors to lose confidence in our reported financial information and may lead to a decline in the trading price of our ADSs.

Our common stock is currently listed on the Tokyo Stock Exchange and other local Japanese stock exchanges, and we have established internal control over financial reporting pursuant to the requirements applicable to companies listed only in Japan. In addition, our ADSs are listed on the New York Stock Exchange (the “NYSE”), making us subject to, among other things, the requirements under the Sarbanes-Oxley Act of 2002 (the “Sarbanes-Oxley Act”). The standards for internal control over financial reporting under the Sarbanes-Oxley Act are significantly more extensive than those applicable to companies listed only in Japan. For example, we are required, pursuant to Section 404 of the Sarbanes-Oxley Act (“Section 404”), to furnish a report by management on, among other things, the effectiveness of our internal control over financial reporting. This assessment must include disclosure of any material weaknesses identified by our management in our internal control over financial reporting, as well as a statement that our independent registered public accounting firm has issued an opinion on our internal control over financial reporting.

We cannot be certain that material weaknesses in our internal control over financial reporting will not develop or be identified. Any failure to achieve and maintain adequate internal control over financial reporting or to implement required, new or improved controls, or difficulties encountered in their implementation could cause material weaknesses or other deficiencies in our internal control over financial reporting in the future. If we are unable to successfully remediate any material weaknesses or other deficiencies in our internal control over financial reporting, the accuracy and timing of our financial reporting may be adversely affected, and investors may lose confidence in our financial reporting, and the price of our ADSs may decline as a result. In addition, if we are unable to continue to meet these requirements, we may not be able to remain listed on the NYSE.

We are subject to additional risk due to uncertainty relating to the calculation of London Interbank Offered Rate ("LIBOR"), Euro Interbank Offered Rate ("EURIBOR") and other reference rates and their potential discontinuance.

The JBIC Loan and the Term Loan Credit Agreement are subject to a floating interest rate calculated in reference to the LIBOR, while the floating rate Euro-denominated senior notes we issued in connection with the Shire Acquisition are subject to floating rate interest calculated in reference to EURIBOR. Interest rate, equity, commodity, foreign exchange rate and other types of indices which are deemed to be benchmarks are the subject of ongoing national, international and other regulatory guidance and proposals for reform. Some of these reforms are already effective while others are still to be implemented. These reforms may cause such benchmarks to perform differently than they have performed in the past or to be discontinued entirely or may have other consequences that cannot be predicted, which could have a material adverse effect on our financial condition or results of operations or require us to seek to amend the terms of the relevant indebtedness, which may require significant additional time, effort or money in the form of consent payments or otherwise, and may not be possible on cost-efficient terms or at all.

The LIBOR that is currently produced in seven tenors across various currencies will cease to be in use by the end of 2021. A number of alternatives to LIBOR have been proposed and may result in interest payments that are higher than expected or that do not otherwise correlate over time with the payments that would have been made on such indebtedness for the interest periods if the applicable LIBOR rate was available in its current form. More generally, any of the foregoing changes, any other changes to LIBOR as a result of national, international and other regulatory guidance and proposals for reform or other initiatives or investigations, or any further uncertainty surrounding the implementation of such changes, could have a material adverse effect on affected indebtedness.

At this time, it is not possible to predict the effect that these developments, any discontinuance, modification or other reforms to LIBOR or any other reference rate may have on LIBOR, other benchmarks or floating rate indebtedness.

Risks Relating to the ADSs

A holder of ADSs has fewer rights than a holder of our common stock has, and a holder of ADSs has to act through the depositary to exercise those rights.

The rights of shareholders under Japanese law to take various actions, including voting their shares, receiving dividends and distributions, bringing derivative actions, examining a company's accounting books and records and exercising appraisal rights, are available only to holders of record. Because the depositary, through its custodian agents, is the record holder of the shares underlying the ADSs, only the depositary can exercise those rights in connection with the deposited shares. Pursuant to the deposit agreement, the depositary will endeavor, to the extent practicable, to make efforts to vote or cause to be voted the shares underlying the ADSs as instructed by the holders and will pay to the holders the dividends and distributions collected from the Company. The depositary and its agents may not be able to send voting instructions to holders of ADSs or carry out their voting instructions in a timely manner. Furthermore, the depositary and its agents will not be responsible for any failure to carry out any instructions to vote, for the manner in which any vote is cast or for the effect of any such vote. As a result, holders of ADSs may not be able to exercise their right to vote. Moreover, in the capacity as an ADS holder, such holder will not be able to bring a derivative action, examine the Company's accounting books or records or exercise appraisal rights except through the depositary.

Rights of shareholders under Japanese law may be more limited than under the laws of other jurisdictions.

Our Articles of Incorporation, Regulations of the Board of Directors, Regulations of the Audit and Supervisory Committee and the Companies Act govern our corporate affairs. Legal principles relating to such matters as the validity of corporate procedures, directors' and officers' fiduciary duties, and shareholders' rights may be different from those that would apply to a non-Japanese company. Shareholders' rights under Japanese law may not be as extensive as shareholders' rights under the laws of other jurisdictions. ADS holders may have more difficulty in asserting their rights as a shareholder than such holders would as shareholders of a corporation organized in another jurisdiction. In addition, Japanese courts may not be willing to enforce liabilities against the Company in actions brought in Japan that are based upon the securities laws of other jurisdictions.

Because of daily price range limitations under Japanese stock exchange rules, a holder of ADSs who has surrendered his or her ADSs in favor of shares of our common stock may not be able to sell his/her shares of our common stock at a particular price on any particular trading day, or at all.

Stock prices on Japanese stock exchanges are determined on a real-time basis by the equilibrium between bids and offers. These exchanges are order-driven markets without specialists or market makers to guide price formation. To prevent excessive volatility, these exchanges set daily upward and downward price fluctuation limits for each stock, based on the previous day's closing price. Although transactions may continue at the upward or downward limit price if the limit price is reached on a particular trading day, no transactions may take place outside these limits. Consequently, a holder of ADSs who has surrendered his or her ADSs in favor of shares of our common stock wishing to sell on a Japanese stock exchange at a price above or below the relevant daily limit may not be able to sell his or her shares at such price on a particular trading day, or at all.

U.S. investors may have difficulty in serving process or enforcing a judgment against us or our directors or executive officers.

We are a limited liability, joint stock corporation incorporated under the laws of Japan. Many of our directors and executive officers reside in Japan, Europe or elsewhere outside of the U.S., and a large portion of our assets and the assets of these persons are located in Japan and elsewhere outside the U.S.. It may not be possible, therefore, for U.S. investors to effect service of process within the U.S. upon us or these persons or to enforce against us or these persons judgments obtained in U.S. courts predicated upon the civil liability provisions of the federal securities laws of the U.S. There is doubt as to the enforceability in Japan, in original actions or in actions for enforcement of judgment of U.S. courts, of liabilities predicated solely upon the federal securities laws of the U.S.

Investors holding less than a full unit of shares will have limited rights as shareholders.

Our Articles of Incorporation provide that 100 shares of our common stock constitute one unit. Although holders of ADSs may withdraw shares of our common stock constituting less than one unit, in connection with the direct holding of the shares of our common stock, the Companies Act imposes significant restrictions and limitations on holders of shares of our common stock that do not constitute a full unit. In general, holders of shares of our common stock constituting less than one unit do not have the right to vote with respect to those shares.

Dividend payments and the amount you may realize upon a sale of our ADSs will be affected by fluctuations in the exchange rate between the U.S. dollar and the Japanese yen.

Cash dividends, if any, in respect of the shares of our common stock represented by our ADSs will be paid to the depositary in Japanese yen and then converted by the depositary into U.S. dollars, subject to certain conditions. Accordingly, fluctuations in the exchange rate between the Japanese yen and the U.S. dollar will affect, among other things, the U.S. dollar amounts a holder of ADSs will receive from the depositary in respect of dividends, the U.S. dollar value of the proceeds that a holder of ADSs would receive upon sale in Japan of the shares of our common stock obtained upon surrender of ADSs and the secondary market price of ADSs.

Our shareholders of record on a given record date may not receive the dividend they anticipate.

The customary dividend payout practice of publicly listed companies in Japan may significantly differ from the practices widely followed or otherwise deemed necessary or fair in foreign markets. We ultimately have a discretion to determine any dividend payment amount to our shareholders of record as of a record date, including whether we will make any dividend payment to such shareholders at all, only after such record date. For that reason, our shareholders of record on a given record date may not receive the dividends they anticipate.

ADS holders may not be entitled to a jury trial with respect to claims arising under the deposit agreement, which could result in less favorable outcomes to the plaintiff(s) in any such action.

The deposit agreement governing the ADSs provides that, to the fullest extent permitted by law, ADS holders waive the right to a jury trial for any claim they may have against us or the depositary arising out of or relating to our shares, the ADSs or the deposit agreement, which may include any claim under the U.S. federal securities laws.

If we or the depositary were to oppose a jury trial based on this waiver, the court would have to determine whether the waiver was enforceable based on the facts and circumstances of the case in accordance with applicable state and federal law. To our knowledge, the enforceability of a contractual pre-dispute jury trial waiver in connection with claims arising under the federal securities laws has not been finally adjudicated by the U.S. Supreme Court. However, we believe that a contractual pre-dispute jury trial waiver provision is generally enforceable, including under the laws of the State of New York, which govern the deposit agreement, or by a federal or state court in the City of New York, which has jurisdiction over matters arising under the deposit agreement. In determining whether to enforce a contractual pre-dispute jury trial waiver, courts will generally consider whether a party knowingly, intelligently and voluntarily waived the right to a jury trial. We believe that this would be the case with respect to the deposit agreement and the ADSs. It is advisable that prospective investors consult legal counsel regarding the jury waiver provision before investing in the ADSs.

As a result, if a holder or beneficial owner of ADSs brings a claim against us or the depositary in connection with matters arising under the deposit agreement or the ADSs, including claims under federal securities laws, such holder or beneficial owner may not be entitled to a jury trial with respect to such claims, which may have the effect of limiting and discouraging lawsuits against us or the depositary. If a lawsuit is brought against us or the depositary under the deposit agreement, it may be heard only by a judge or justice of the applicable trial court, which would be conducted according to different civil procedures and may result in different outcomes than a trial by jury would have, including outcomes that could be less favorable to the plaintiff(s) in any such action.

Nevertheless, if this jury trial waiver is not enforced under applicable law, an action could proceed under the terms of the deposit agreement with a jury trial. No condition, stipulation or provision of the deposit agreement or the ADSs serves as a waiver by any holder or beneficial owner of ADSs or by us or the depositary of compliance with any substantive provision of the U.S. federal securities laws and the rules and regulations promulgated thereunder.

Item 4. Information on the Company

A. History and Development of the Company

We are a global, values-based, research and development ("R&D") driven biopharmaceutical company with operations in approximately 80 countries. We bring highly innovative, life changing medicines to patients across the globe, with prescription drugs marketed directly or through our partners in approximately 100 countries worldwide. Our global workforce is committed to bringing better health and a brighter future to patients. We develop and market pharmaceutical products in gastroenterology ("GI"), rare diseases including rare metabolic, rare hematology and heredity angioedema, oncology, neuroscience, as well as Plasma-Derived Therapies ("PDT") and vaccines. We are also committed to our corporate social responsibility program, which is dedicated to global health, and our access to medicine strategy, which aims to increase access to innovative and potentially lifesaving medicines for patients with some of the highest unmet medical needs across the world.

Our 239-year history started in 1781, when Chobei Takeda began selling traditional Japanese and Chinese medicines in Doshomachi, Osaka. After Japan's Meiji Restoration opened the country to increase overseas trade in the late 1860s, we were one of the first companies to begin importing western medicines into Japan. In 1895, we began our pharmaceutical manufacturing business, and our research division was formed in 1914, allowing us to begin to discover our own pharmaceutical products. In 1925, we were incorporated as Chobei Takeda & Co., Ltd. and our name was later changed to Takeda Pharmaceutical Company Limited. In 1949, our shares were listed on the Tokyo and Osaka stock exchanges. We began expanding into overseas markets in the 1960s, first in Asia and, subsequently, other markets around the world. We began enhancing our overseas business infrastructure in the late 1990s, with the formation of new subsidiaries in the U.S. and Europe.

Since 2014, our efforts have been focused on enhancements to our R&D capabilities and successful cross-border acquisition activities and post-acquisition integration. For example, in February 2017, we acquired ARIAD Pharmaceuticals, Inc., a commercial-stage biotechnology company, to obtain late stage assets for the treatment of cancer. In July 2018, we acquired TiGenix NV, an advanced biopharmaceutical company developing novel stem cell therapies for serious medical conditions, with the aim to bring new treatment options to patients with gastrointestinal disorders.

Most recently, we completed the acquisition of Shire in January 2019. With the Shire Acquisition, we took a major step in our development into a global pharmaceutical company. The Shire Acquisition allowed us to create a global, values-based, R&D-driven biopharmaceutical company with an attractive geographic footprint including a significantly increased presence in the U.S., an important and innovation-driven market. Specifically, the Shire Acquisition strengthened our core therapeutic areas, bringing together Takeda and Shire's complementary positions in GI and neuroscience and providing leading positions in rare diseases and PDT to complement Takeda's previously existing strength in oncology and focused efforts in vaccines. It also contributed to a highly complementary, robust, modality-diverse pipeline and a strengthened R&D engine focused on innovation.

During the three fiscal years ended March 31, 2020, we have also divested several businesses and assets in non-core areas. We will continue divesting businesses and assets that are not core to our operations to accelerate deleveraging. See Item 5.A, Operating Results, for further details on divested businesses and assets.

Our principal capital expenditures during the three fiscal years ended March 31, 2020 consisted of additions to property, plant and equipment and additions to intangible assets. In the fiscal years ended March 31, 2018, 2019 and 2020, excluding acquisitions, we made capital expenditures (consisting of the additions to property, plant and equipment and intangible assets recorded on our consolidated statements of financial position) of 124.1 billion JPY, 244.6 billion JPY and 246.3 billion JPY, respectively, including the following highlights:

- In the fiscal year ended March 31, 2018, we invested 17.9 billion JPY to construct our new global headquarters in Tokyo. We also invested 11.4 billion JPY to purchase manufacturing equipment at our German subsidiary, Takeda GmbH, including 4.9 billion JPY in equipment for manufacturing of vaccines for dengue fever.
- In the fiscal year ended March 31, 2019, we entered into an additional 20-year extension agreement (from 2030 to 2050) for our two leased properties in Cambridge, Massachusetts. The total lease liability for these properties including the renewal option that we are reasonably certain to exercise is 88.8 billion JPY as of March 31, 2019.
- In the fiscal year ended March 31, 2020, we invested in expanding our plasma collection center network, with the addition of 32 new centers in the U.S. and Europe.

We currently have various capital expenditures projects in process, including the expansion of production capacity of our plasma manufacturing network.

The address of our global head office is 1-1, Nihonbashi-Honcho 2-Chome, Chuo-ku, Tokyo, 103-8668, Japan; telephone number: 81-3-3278-2306. Takeda's agent in the U.S. in connection with this annual report is Takeda Pharmaceuticals U.S.A. Inc., 99 Hayden Avenue, Lexington, MA 02421 U.S.A., telephone number: 1-617-349-0200.

The SEC maintains an Internet site that contains reports, proxy and information statements, and other information regarding issuers that file electronically with the SEC at www.sec.gov. As a foreign private issuer, we are exempt from the rules under the Securities Exchange Act of 1934 (the "Exchange Act") prescribing the furnishing and content of proxy statements to shareholders. Our corporate website is www.takeda.com.