# Case 2

# Vision 2020: Takeda and the Vaccine Business

*"Our goal is to advance global public health through new products and technologies."*

—Yasuchika Hasegawa, President and Chief Executive Officer of Takeda

One of Japan's most respected business leaders, Mr. Yasuchika Hasegawa was, in 2013, leading the transformation of Takeda Pharmaceuticals from a traditional Japanese company with a global footprint into a global company with a rich Japanese heritage. A 33-year veteran of Takeda, Hasegawa was appointed president of the company in 2003 and chief executive officer in 2009. In 2011, he was also appointed chairman of the Keizai Doyukai (Japan Association of Corporate Executives). By 2013, Hasegawa's efforts to globalize Takeda were coming to fruition and Takeda was in the midst of implementing Vision 2020, its long-term plan to guide the company toward sustainable growth. Importantly, Takeda's Vision 2020 included developing a global vaccine business.

## 2.1 Company Background

Takeda Pharmaceuticals was founded in 1781 by Chobei Takeda I when he began selling Chinese and Japanese medicines he purchased from wholesalers to Japanese consumers in Osaka. Chobei Takeda I became known for the consistently high quality of his products as well as his integrity in business dealings. These ethics were passed down through the generations of the Takeda family, and their business grew. Chobei II and Chobei III both expanded their business in Osaka, and they upheld the reputation of the Takeda family through strict written codes of honor. During Japan's Meiji Restoration,[a] Chobei IV spearheaded the formation of a cooperative importing company based in Yokohama called Maruhon, based in Yokohama, to expand the availability of Western medicines in Japan. Chobei IV also began Takeda's manufacturing business with the acquisition of Uchibayashi Drug Works in 1895. In 1915, Chobei V established the Takeda Pharmaceutical manufacturing plant, and the Drug Discovery Division was established 1918. In 1950, Takeda began selling Japan's first multivitamin, Panvitan®, which was a boon to public health in the war-ravaged, malnourished, and vitamin-deficient Japanese society of the time.

In 1962, Takeda established a manufacturing and marketing company in Taiwan, which was followed by the launch of manufacturing and marketing satellites across Southeast Asia, including operations in Thailand (1969) and Indonesia (1971). In 1978, Takeda entered into a pharmaceutical marketing joint venture in France, followed by the establishment of its Europe R&D Center in 1988. Takeda commenced a joint research partnership with Abbott Laboratories in the U.S. in 1977, and formalized this partnership in a sales and marketing entity named TAP Pharmaceuticals in 1985. Through TAP, Takeda and Abbott launched blockbuster drugs Lupron (a treatment for prostate cancer) and Prevacid (an anti–peptic ulcer agent) in 1985 and 1995, respectively. Around the same time, Actos was launched as an oral antidiabetic drug in both Japan and the U.S., and became a mainstay of Takeda's business.

a The Meiji Restoration was the series of events that restored imperial rule to Japan under the Meiji emperor. It lasted from 1868 to 1912 and was responsible for the modernization of Japan.

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**EXHIBIT 1 Top Global Consumer Health[a] Companies, 2007–2012**

| Company[b] | 2007 Rank | 2008 Rank | 2009 Rank | 2010 Rank | 2011 Rank | 2012 Rank | 2012 Market Share |
|---|---|---|---|---|---|---|---|
| Johnson & Johnson | 1 | 1 | 1 | 1 | 1 | 1 | 3.6% |
| Bayer AG | 3 | 3 | 3 | 3 | 3 | 2 | 3.0% |
| GSK | 2 | 2 | 2 | 2 | 2 | 3 | 2.5% |
| Novartis | 5 | 4 | 4 | 4 | 4 | 4 | 2.3% |
| Amway | 6 | 6 | 5 | 5 | 5 | 5 | 2.3% |
| Pfizer | 12 | 12 | 6 | 6 | 6 | 6 | 2.2% |
| Herbalife | 9 | 8 | 8 | 8 | 8 | 7 | 2.2% |
| Sanofi | 11 | 11 | 10 | 7 | 7 | 8 | 2.1% |
| Procter & Gamble | 8 | 10 | 11 | 12 | 12 | 9 | 1.7% |
| Takeda | 20 | 20 | 19 | 20 | 16 | 16 | 0.9% |

*Source: Adapted from "Consumer Health: Takeda Pharmaceutical Co. Ltd.," Euromonitor Passport, 2012.*

[a] Consumer Health total is the sum of OTC, Sports Nutrition, Vitamins and Dietary Supplements, Weight Management, and the subcategories of Herbal Medicinal Teas and Herbal Smoking Cessation Aids.

[b] Includes only branded manufacturers. Private label had 6.7%, and Others had 40.3%

Before the establishment of TAP, Takeda had focused primarily on Japan's pharmaceutical market and its subsidiaries in Asia. However, the company gradually expanded its presence in North America and Europe throughout the 1990s and 2000s. The company leveraged excess cash and favorable exchange rates in 2008 to expand its oncology research capabilities through the acquisition of Millennium Pharmaceuticals, and it did so again in 2011 to expand its global footprint through the acquisition of the Norwegian pharmaceutical company Nycomed.

## 2.1a Acquisitions and Global Growth

In March 2008, Takeda acquired the Japanese operations of the American pharmaceutical company Amgen, including the rights to several of Amgen's pipeline candidates for the Japanese market.[1] In the same month, Takeda and Abbott Laboratories announced the conclusion of their 30-year-old joint venture, TAP Pharmaceuticals. Abbott acquired the U.S. rights to the drug Lupron, while Takeda received the rights to Prevacid and TAP's pipeline candidates. In April 2008, Takeda began acquiring companies to expand its global operations, beginning with its acquisition of Millennium Pharmaceuticals, as referenced above. Located in Cambridge, Massachusetts, Millennium specialized in cancer drug research and development. Through Millennium, Takeda acquired Velcade, a drug indicated for hematological malignancies, as well as a portfolio of pipeline candidates in the oncology and inflammation areas.[2] Separate from Takeda's excellence in research and development functions, in 2013 Fortune ranked its Millennium subsidiary as one of the 100 best companies to work for in the United States.[3] Millennium boosted Takeda's global research capabilities and provided a model for cultural and functional integration for future acquisitions.

In September 2011, Takeda acquired Nycomed for $13.7 billion.[4] The acquisition required Takeda to absorb a portfolio centered on branded generics and private-label products. (Nycomed's product portfolio included no blockbuster drugs.) Nycomed focused heavily on licensing relatively small products (averaging $10 million in annual sales) that had already gained market acceptance and then worked to extend their product life cycles. In addition, the acquisition of Nycomed increased Takeda's global reach from 28 countries to over 70 countries. The skill of Nycomed in tailoring portfolios to individual countries and regions gave Takeda valuable expertise as well as a sales and marketing infrastructure in emerging markets. These commercial operations could then be leveraged to market branded generics and other Takeda products that were no longer under patent protection.

In 2012, Takeda acquired three separate U.S.-based research and development companies to expand its pipeline in key areas: URL Pharma, LigoCyte

Pharmaceuticals, and Evoy Therapeutics.[5] In July 2012, Takeda purchased the Brazilian pharmaceutical company Multilab Indústria e Comércio de Produtos Farmacêuticos for $246 million,[6] further expanding its product portfolio and marketing presence in Brazil, a key strategic region for Takeda's emerging markets strategy.

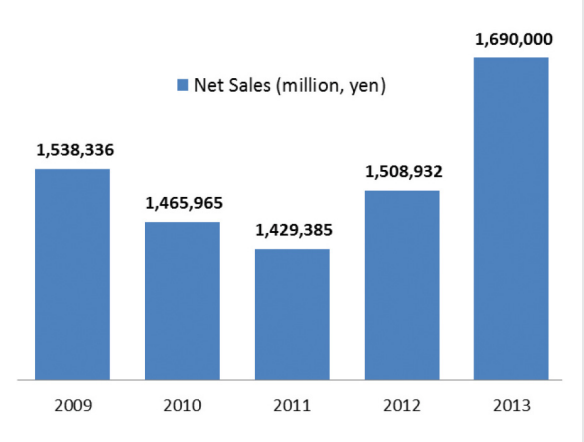
By 2013, Takeda was the largest Japanese pharmaceutical company in annual revenues and the 15th largest pharmaceutical company worldwide.[7] (See Exhibit 1 for a list of top pharmaceutical companies.) In fiscal year 2012, 735 billion yen[b] of Takeda's total sales of 1,557 billion yen were in Japan (in contrast to 2007, when 681 billion yen of Takeda's total net sales of 1,375 billion yen were in Japan). Takeda's second and third largest markets were, respectively, the Americas, with 424 billion yen in sales (27.2%), and Europe, with 315 billion yen in sales (20.2%). (See Exhibit 2 for Takeda's sales, 2009–2013.) Between fiscal year 2009 and fiscal year 2012, Takeda's total revenues declined due to the loss of patent exclusivity on key products, including Prevacid (2009)[8] and Actos (2012).[9] Its net operating margin also declined as a result, to reach a five-year low of 7.9% in 2012 (See Exhibit 3 for Takeda's financials.)

In 2013, Takeda's product portfolio comprised patent-protected prescription drugs, branded generics,[c] vaccines, and over-the-counter (OTC) medicines. Takeda's product portfolio was aligned to six therapeutic areas: Cardiovascular & Metabolic, Oncology, Central Nervous System, Immunology & Respiratory, General Medicine (Gastrointestinal & Genitourinary), and Vaccines. In fiscal year 2012, about 90% of Takeda's revenue stemmed from prescription drug sales. (See Exhibit 4 for Takeda's top five prescription drug products.) Like most pharmaceutical companies, Takeda used in-licensing and R&D alliances to expand its product portfolio beyond internally developed products. In 2012 alone, Takeda licensed two drugs developed by U.S.-based firms and one from a Danish firm to sell in Japan.

Takeda's series of global acquisitions brought in a large number of non-Japanese employees and increased the company's geographic reach dramatically. In fiscal year 2007, 44% of Takeda's workforce of over 15,000 was located in Japan; by fiscal year 2012, the proportion

b In 2013, 100 Japanese yen was equal on average to $1.00.
c Branded generics were pharmaceutical products for which patents had expired.

## EXHIBIT 2 Takeda's Net Sales, 2009–2013[a]




*Source: Company documents*
[a] 2013 net sales are estimated.

## EXHIBIT 3 Takeda Selected Financials, Fiscal 2010–2012 (yen, billion)

| | Fiscal 2012 | Fiscal 2011 | Fiscal 2010 |
|---|---|---|---|
| Net sales | 1,557 | 1,509 | 1,419 |
| Cost of sales | 448 | 433 | 318 |
| SG&A | 987 | 811 | 735 |
| Operating income | 123 | 265 | 367 |
| Net income | 131 | 124 | 248 |
| R&D expenses | 324 | 282 | 289 |
| Capital expenditures | 283 | 126 | 149 |

*Source: Company Documents*

**EXHIBIT 4 Takeda's Top Five Prescription Drug Products, Fiscal 2012**

| Company Brand Rank | Brand | Focus | Fiscal 2012 Sales (yen, billion) |
|---|---|---|---|
| 1 | Blopress | Hypertension | 169.6 |
| 2 | Actos | Diabetes | 122.9 |
| 3 | Leuplin | Prostate/Breast Cancer | 116.5 |
| 4 | Prevacid | Peptic Ulcers | 110.2 |
| 5 | Velcade | Multiple Myeloma | 72.9 |

*Source: Adapted from "Consumer Health: Takeda Pharmaceutical Co. Ltd.," Euromonitor Passport, 2012..*

overseas had increased to 69% of Takeda's over 30,000 employees. Takeda maintained its global headquarters in Osaka and Tokyo.

## 2.1b Corporate Social Responsibility and Access to Medicines

Takeda's responsibility to provide affordable and accessible healthcare solutions to people in need was integral to the company's core business practices. (See Exhibit 5 for Takeda's Corporate Social Responsibility (CSR) and sustainable business model.) Takeda's mission involved "striving towards better health for people worldwide through leading innovation in medicine," and its CSR policy stated: "We believe that the essence of CSR for Takeda lies in developing outstanding pharmaceutical products in accordance with the principles of our corporate philosophy of 'Takeda-ism' (Integrity: Fairness, Honesty and Perseverance). From another perspective, we are very aware that our sustainability can exist only when a sustainable and healthy society is assured."[10] Among other features of its CSR policy, the company acknowledged the role of pharmaceutical companies in promoting sustainable societies by providing access to medicines (ATM) and targeting areas of medical need that had previously gone unfunded and unresearched due to lack of interest and urgency in the developed world.

**Strategic Philanthropy** Understanding the importance of ATM from the viewpoint of a global pharmaceutical company, as aligned with the Millennium Development Goals (MDGs) of the United Nations, Takeda started its CSR actions from a strategic philanthropy approach. In 2009, Takeda initiated a partnership program, called the "Takeda-Plan Access to Healthcare Program," with Plan Japan, an affiliate of Plan International, a globally influential NGO in four Asian countries where it operated. In 2010, working in tandem with Japanese government initiatives, Takeda created a

**EXHIBIT 5 Takeda's CSR and Sustainability Model, 2013**


*Source: Company documents*

10-year grant program dubbed the "Takeda Initiative." This initiative supported the Global Fund to Fight AIDS, Tuberculosis and Malaria (the Global Fund) for healthcare workers in three African countries.[d] Following a third-party evaluation of Takeda's ATM performance, the company decided to shift its ATM mind-set from one of strategic philanthropy as a corporate citizen to a mind-set that incorporated ATM activities as a part of its core business model.

**Access to Medicine Index** In 2012, Takeda was included in the "Access to Medicine Index," a ranking of global pharmaceutical companies jointly funded by the Bill and Melinda Gates Foundation and the governments of the UK and the Netherlands.[11] Twenty companies were ranked according to their performance in seven key areas[e] with the goal of increasing the availability of medicines worldwide. Takeda ranked 18th on the index, yet it was the second-highest-ranking Japanese company.[f] Takeda aimed to increase its efforts to make medicine widely available in the hope of raising the global profile of Japanese pharmaceutical companies. The Bill and Melinda Gates Foundation funded efforts to increase ATM worldwide via programs like Medicines for Malaria, the Global Alliance for Tuberculosis, and the Malaria Vaccine Initiative. While the foundation provided funding for the distribution of medicines,[g] Takeda believed that additional investment was needed in basic and applied research for the development of life-saving medicines. In an effort to meet this need, Takeda worked with key partners to establish the Global Health Innovative Technology (GHIT) Fund.

**Takeda and the GHIT Fund** The GHIT Fund was launched in April 2013 as a nonprofit partnership between the Bill and Melinda Gates Foundation, the Japanese government, and five Japanese pharmaceutical companies[h] to focus on investing in health technologies designed to defend against infectious diseases. Investment in infectious diseases was relatively low throughout the pharmaceutical industry, as products targeted at patients with chronic conditions in the developed world were typically more profitable. While the rate of chronic diseases was also increasing in the developing world, infectious diseases continued to disproportionately impact developing countries.

The fund provided grants to nonprofits and academic institutions that partnered with a Japanese organization to commercialize products related to global health issues. The partners all contributed to the fund: the five Japanese companies committed $5 million over five years (for a total fund of $25 million), the Bill and Melinda Gates Foundation pledged $25 million, and the Japanese government contributed $50 million (based on the "Strategy for Global Health Diplomacy," the "Healthcare and Medical Strategy," and the "Japan Revitalization Strategy"). The selection committee for the disbursal of GHIT Fund grants was composed of an independent panel of experts, and the council of the GHIT Fund included the chief executives of the partner companies as well as representatives from government.

In 2013, the GHIT Fund had 13 partnerships under way for drug discovery, 3 of which involved Takeda.[i] Through GHIT Fund grants, Takeda also participated in two antimalarial projects with the Geneva-based product-development partnership Malaria Medicines Venture. The GHIT Fund helped Takeda to expand its contribution to address unmet needs in emerging markets (including vaccines). The fund aimed to move from the presentation of concept to the delivery of grant money to successful applicants in only 18 months. First-round grants awarded by the fund typically went to later-stage products that had a good chance of commercialization within five years. All drugs and health technologies developed through the GHIT Fund would be distributed on a "no gain, no loss" basis.

d Specifically, Nigeria, Tanzania, and Senegal.

e The seven key areas were general access to medicine management; public policy and market influence; research and development; pricing, manufacturing, and distribution; patents and licensing; capability advancement in product development and distribution; and product donations and philanthropic activities.

f Three Japanese companies—Eisai Co. Ltd., Daiichi Sankyo Co. Ltd., and Astellas Pharma Inc.—held the 15th, 19th, and 20th rankings, respectively.

g The cost of distributing medicines, particularly vaccines, to developing countries was not insignificant. Vaccines had to be transported and refrigerated in a narrow temperature range in order to maintain their efficacy.

h Astellas Pharma Inc., Daiichi Sankyo Co. Ltd., Eisai Co. Ltd., Shionogi & Company Ltd., and Takeda Pharmaceutical Co. Ltd.

i Through the GHIT Fund, Takeda signed bilateral agreements with the Global Alliance for TB Drug Development (TB Alliance) in a search for compounds of tuberculosis, with the Medicines for Malaria Venture (MMV) to seek out new candidates for treating malaria, and with the Drugs for Neglected Diseases initiative (DNDi) as part of its effort to find new treatments for three neglected tropical diseases.

### 2.1c From Participation to Collective Action

Since October 2012, all ATM-related issues were reviewed under the Global Health Project, a cross-department initiative led by Dr. Tadataka Yamada, Takeda's director and chief medical and scientific officer. For example, the project team reviewed the Guiding Principles on Access to Healthcare (GPAH) formulated by Takeda and the 12 other global drug companies that were members of the BSR (Business for Social Responsibility) Healthcare Working Group. The GPAH, endorsed by Takeda in July 2013, covered five core areas: collaboration, research and development, expanding availability of healthcare services, developing health systems resources, and respecting human rights.

## 2.2 Vision 2020

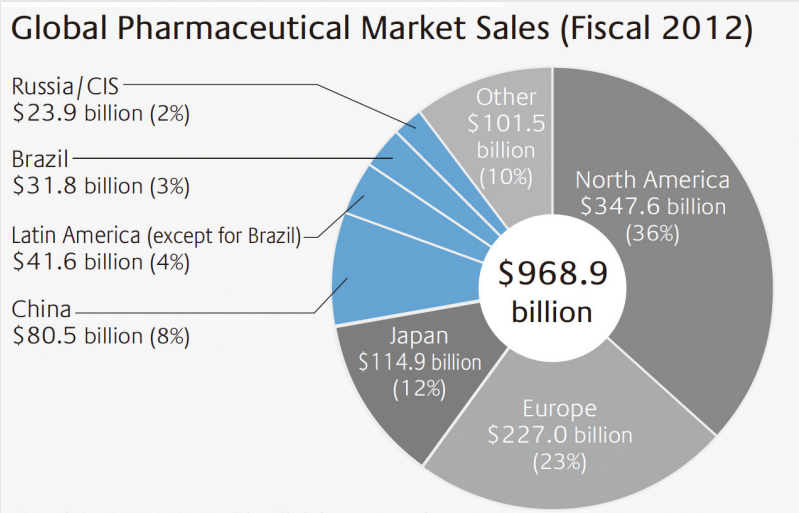
In 2011, Takeda identified several potential threats to its revenues and profits: an immediate "patent cliff," given that several of its leading pharmaceuticals would soon reach the end of their patent protection; slowing growth in Takeda's three largest markets (Japan, the Americas, and Europe); and single-payer insurance systems, like Japan's National Health Insurance, which were beginning to promote greater use of generic products over branded products.[j]

At the same time, Takeda was also in the process of integrating Nycomed's operations. Takeda's leadership had diligently investigated Nycomed's assets and corporate values before the acquisition to ensure a good fit with Takeda's core values. Hasegawa believed that integrating two large corporations with different corporate cultures required a "common vision" and "team spirit" to guide the combined group. Hasegawa also believed that any new vision should build upon the long-existing values of "Takeda-ism" (Integrity: Fairness, Honesty and Perseverance) developed over the course of the company's 230-year history.

Hasegawa sought to shift Takeda from a business dependent upon a limited number of markets to a truly global company. "If you are a global company, you have to have a presence in emerging markets to grow," he stated. (See Exhibit 6 for pharmaceutical industry revenue by region in 2012.) He recognized that the Nycomed

j In April 2012, the Japanese government revised the National Health Insurance drug prices and medical service fees to encourage greater usage of generic drugs

**EXHIBIT 6 Global Pharmaceutical Industry Sales by Region, Fiscal 2012**




*Source: Company documents.*

acquisition presented an opportunity to develop a new global strategy for Takeda. At the same time, the size of the integration and the overnight expansion into many new markets posed significant challenges.

## 2.2a Developing Vision 2020

The process of developing the new, comprehensive strategic vision that Hasegawa desired was unusual in Japan and took Takeda's leadership one and a half years to complete. The Global Leadership Committee (GLC), composed of nine individuals[k] spanning the company's functions, began by reviewing their long-term goals for the company. Unifying the visions for each function into a singular vision for the company required careful discussion, and it was difficult for some on the committee to shift their thinking from being a Japanese company to being a global company. Despite that, what brought all the GLC members together was their shared pride in Takeda's long history of providing quality medicines to patients.

After working through the differing perspectives, the committee began to draft the key components of their vision. "Setting 2020 as the target year, we conducted in-depth conversations with senior managers on how we envisioned Takeda in 2020," said Mr. Yasuhiko Yamanaka, the company's managing director and the Vision 2020 project leader. The committee produced five vision scenarios, each with 10 subpoints, depicting the likely state of the industry in 2020 and the role that Takeda would play.

Next, the GLC sought input from the 370 department heads via town hall meetings, which were conducted at seven company locations. The five vision scenarios aligned with each location's thinking, but, depending upon the location, the priorities within the scenarios differed. This process resulted in an important insight. All locations agreed that any new vision and strategy must help to "build a company for a society where global citizens could live happily, in better health."[12] Takeda realized that people who consumed its products wanted not just the safety and efficacy of those products; ultimately, the people Takeda served sought a better quality of life.

Collecting feedback helped Takeda's leadership crystallize Vision 2020 into one key phrase: "Better Health, Brighter Future." "Better Health" was intentionally left broad so as to include activities ranging from preventing disease to managing illness. Management believed that the phrase reflected Takeda's strengths as well as conveyed a vision that was both aspirational and able to evolve as the company met new market and industry conditions. "Brighter Future" reflected the increasing emphasis by consumers on quality of life and productivity outcomes[l] rather than just therapeutic efficacy. The phrase originated from Takeda's Head of Corporate Communications, and the committee then agreed to three subpoints: Committed to Improving Health, Powered by Passion, and Strength from Diversity. (See Exhibit 7 for the Vision 2020 plan.) According to Yamanaka, the Vision 2020 project leader:

> *The result of this process is a definitive statement of what we aspire to be as the new Takeda—a new corporate vision that we have named "Vision 2020." This builds on Takeda's 230-year commitment to patients as well as our passion by recognizing that we take our strength from diversity to fully understand healthcare needs around the world and contribute to people and society with a sense of urgency. Vision 2020 will guide us as we act on our core values, which we call Takeda-ism, in the pursuit of our corporate mission to "strive towards better health for people worldwide through leading innovation in medicine."*

## 2.2b Execution of the Mid-Range Growth Strategy to Achieve Vision 2020

After developing Vision 2020, Takeda created the Mid-Range Growth Strategy, which launched in April 2013. The Mid-Range Growth Strategy called for Takeda to execute management strategies based on three core principles: Globalization, Diversity, and Innovation. Takeda recognized that a redesign of its business operating model was necessary to manage its now global operations and to better incorporate its CSR values into the business strategy. Hasegawa shared the following:

> *Under the new Mid-Range Growth Strategy, we will create and sustain corporate value by conducting our business according to the core principles of Globalization, Diversity, and Innovation, while also further enhancing our corporate social responsibility activities to respond to the demands of society. Takeda's management team and diverse global workforce of 30,000*

k Four of the members were non-Japanese, and one of those four was female (from Millennium).

l For example, fewer days off work.

## EXHIBIT 7 Takeda's Vision 2020 Plan, 2013

### Mission

We strive towards better health for people worldwide through leading innovation in medicine.

### Vision 2020

# Better Health, Brighter Future

For more than 230 years, we have been serving society with innovative medicines and helping patients reclaim valuable moments of life from illness. Now, with new healthcare solutions from prevention to care and cure, we are determined to help even more people enjoy their lives to the fullest.

We continue to transform the future of healthcare by unifying our strengths as "Global One Takeda." We are a diverse organization committed to working with local communities to fully understand their needs and deliver industry-leading solutions with a sense of urgency, dedication and unparalleled efficiency.

Our passion for healthcare and commitment to improving lives will enable us to make the next 230 years healthier and brighter for people around the world.


### Takeda-ism and Values

Takeda-ism is the unchanging set of **core values** that guides all our activities. We pledge to act with **Integrity**—comprising **Fairness**, **Honesty** and **Perseverance**—at all times, especially when facing difficulties or challenges.

In our day-to-day work, we focus on the following **values** while upholding the highest ethical standards:

- **Diversity**
- **Commitment**
- **Passion**
- **Teamwork**
- **Transparency**
- **Innovation**


*Source: Company documents.*

*employees will make a concentrated effort to quickly overcome our decreased profitability due to generic replacement of blockbuster products, all while remaining committed to the corporate philosophy of "Takeda-ism" (Integrity: Fairness, Honesty and Perseverance), which lies at the heart of all our business activities.*

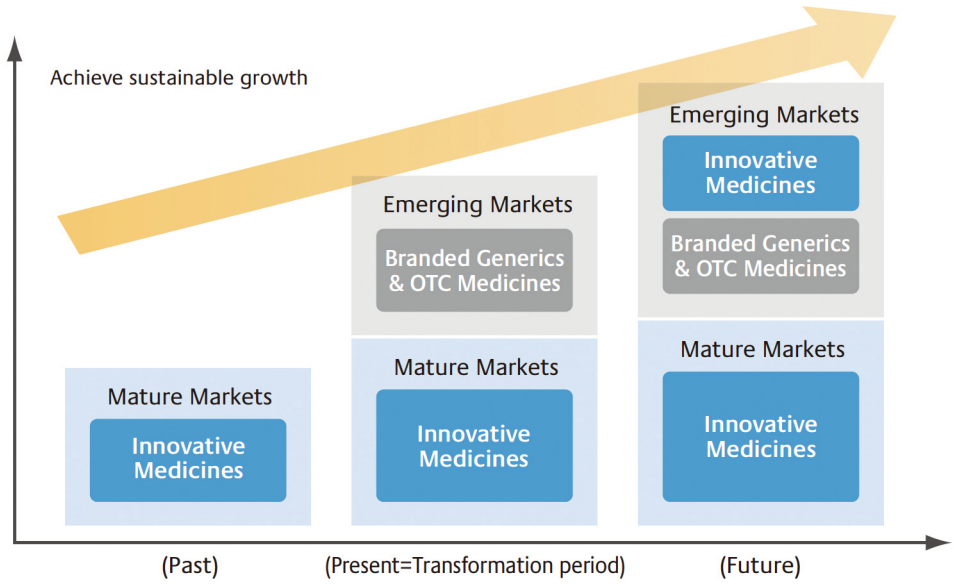
Takeda's Mid-Range Growth Strategy elaborated on its three foundational components:

- **Globalization:** Takeda focused on building its business in emerging markets (mainly in Russia/CIS,[m] Brazil, and China) with its existing portfolio of branded generics and OTC medicines. It planned to progress in the Japanese, European, and U.S. markets with fast commercialization of new products. (See Exhibit 8 for Takeda's globalization strategy.)
- **Diversity:** Takeda committed itself to build a creative and innovative corporate culture by having employees from different countries, cultures, and backgrounds.
- **Innovation:** Takeda focused on R&D innovation for its six therapeutic areas, improving the productivity of the R&D process, and establishing an efficient operating model (with a particular focus on leveraging Nycomed's infrastructure).

Dr. Yamada believed it imperative to improve the operational efficiency of Takeda's R&D pipeline. Prior to his joining Takeda, the development of new pharmaceuticals, from the creation of the molecule to the first human trial, required 39 months on average. In Dr. Yamada's prior experience at GlaxoSmithKline (GSK), the same process could be completed in 16 months on average. Dr. Yamada settled on a three-pronged strategy to increase efficiency: create drug discovery units aligned with Takeda's therapeutic units (in order to apply resources more efficiently); set objectives around value creation rather than milestones (the "distance" between R&D milestones was often inconsistent and did not reflect a project's true progress); and accelerate innovation by awarding early funding to promising projects (if successful, the project was added to the pipeline, and roughly 70% of projects funded in the first round made it in).

m The Commonwealth of Independent States (CIS) was composed of Azerbaijan, Armenia, Belarus, Georgia, Kazakhstan, Kyrgyzstan, Moldova, Russia, Tajikistan, Turkmenistan, Uzbekistan, and Ukraine.

**EXHIBIT 8 Takeda's Mid-Range Strategy: Globalization, 2013**




*Source: Company documents.*

Takeda's revised approach to testing new products was designed to accelerate innovation; rather than moving every drug candidate through Phase I, Phase II, and Phase III clinical trials sequentially, the company shifted to a system that better determined which products would be successful at an early stage. "We will perform key experiments that will tell us if a product will succeed or not early in the process. Success in these key experiments will give us more confidence with later-phase studies," said Dr. Nancy Joseph-Ridge, the general manager of Takeda's Pharmaceutical Development Division.

### 2.2c *Applying Vision 2020 to Emerging and Established Markets*

Takeda's projected compound annual (revenue) growth rate (CAGR) in emerging markets from 2013 to 2017 was at least 15%. Takeda aimed to achieve a CAGR of 20% for operating income during this period, which meant that the firm needed to not only enter emerging markets but to do so with a superior portfolio of products. Branded generics and OTC products were expected to drive short- to medium-term growth in emerging markets, while new products were expected to have a greater role in long-term growth, particularly new drugs and vaccines tailored to the needs of individual markets. "In Vision 2020, we state that our business objective is to pursue innovative medicines as well as high-quality branded generics (branded ethical products for which patents have expired), life-saving vaccines, and OTC medicines to help as many people as we can, as soon as we can," said Hasegawa.

In its emerging markets strategy, Takeda chose to focus on Russia/CIS, Brazil, and China because of the alignment of the medical needs in these particular regions to Takeda's product portfolio. In 2012, Takeda grew faster than the overall market in each of these three regions, partly because it invested to support future expansion.

In mature markets, new products that addressed unmet needs were expected to drive the majority of the growth, although relatively high regulatory standards constrained the speed of new product launches in those markets. In the U.S., Takeda elected to take a slightly broader approach by shifting marketing resources from its existing blockbuster drugs to a more diverse portfolio that would include four new products (vortioxetine, vedolizumab, alogliptin, and Contrave) by 2014. In all developed markets, Takeda sought to increase revenue to cover profit losses incurred by those drugs that had gone off patent and subsequently faced fierce competition from generics.

## 2.3 The Vaccine Business

Vaccines enhanced the body's defenses to specific diseases by exposing the immune system to components of the relevant virus or bacteria. Such exposure spurred the development of antibodies, which prevented individuals from falling ill when exposed to the disease in the future. Vaccinated individuals typically required 2 to 10 days following the injection to develop antibodies, and the protection afforded by vaccines could last for years.[13] From a public health and consumer standpoint, vaccines offered tremendous value, as they prevented many from falling sick to begin with (and thus reduced the need for additional health services). A large number of lethal diseases had been eliminated through the proliferation of vaccinations. (See Exhibit 9 for a list of diseases eliminated as of 2011.)

**EXHIBIT 9 Diseases Eliminated through Vaccination, 2011**

| Disease | 20th Century Annual Deaths | 2011 Deaths |
|---|---|---|
| Smallpox | 48,164 | 0 |
| Diphtheria | 175,885 | 0 |
| Tetanus | 1,314 | 36 |
| Polio (paralytic) | 16,316 | 0 |
| Measles | 503,282 | 222 |
| Mumps | 152,209 | 158 |
| Rubella | 47,745 | 4 |
| Congenital rubella | 823 | 0 |

*Source: Adapted from Alison Sahoo, "What's Next in Vaccines," Kalorama Information Market Intelligence Report, June 2012, via MarketResearch.com, accessed January 2014.*

## 2.3a Vaccine Market Size and Growth

In 2010, 23 billion vaccine doses were produced worldwide, with demand expected to reach over 35 billion doses by 2015.[14] Vaccines represented a small portion of total global pharmaceutical sales (~2%)[15] but were growing faster than total pharmaceuticals (estimated 2011 to 2016 CAGR of 8.9% versus 6.2%).[16] In 2011, the global market for vaccines totaled $19.8 billion at manufacturer prices (expected to increase to $30.4 billion by 2016),[17] with pediatric vaccines accounting for $11.1 billion and adult vaccines for $8.7 billion.[18] The adult segment included especially vulnerable subgroups such as pregnant women and the elderly. Pediatric vaccines and vaccines for adult travelers were expected to grow faster, with estimated CAGR between 2011 and 2016 of 9.0% per year and 12.2% per year, respectively.[19] (The estimated CAGR between 2011 and 2016 for all adult vaccines was 8.9% per year.)[20] In 2013, there were more than 120 new vaccine candidates in the development pipeline, roughly half of which would be of importance to developing markets.[21]

Growth in the vaccine industry was driven by increasing demand and increasing profitability. Growing consumption was driven by a variety of factors:[22]

- **Aging Populations:** Seniors were more susceptible to vaccine-preventable diseases like influenza than the general population, and companies and policymakers were placing increasing emphasis on immunization for the elderly.
- **Mobility:** As travel increased, diseases historically prevalent in remote areas became global.
- **Increasing Usage of Vaccines:** People were coming to accept that vaccinations were for adults as well as children.
- **Usage of Vaccines in More Countries:** The World Health Organization and others continued to expand immunization programs into new countries with previously poor vaccination records.
- **Rising Promotion and Public Awareness:** Direct-to-consumer advertising and other communications programs increased consumer awareness of the importance of vaccines.

Vaccines were also profitable for both healthcare payers and manufacturers:

- **Cost-Effectiveness:** Vaccines reduced costs for healthcare payers by preventing selected diseases. The estimated healthcare savings for every dollar invested in vaccination was between $7 and $20.23
- **Advancing Technology:** New technologies decreased the cost of producing effective vaccines.
- **Lack of Generics:** The vaccine industry had fewer generic alternatives to branded products.

## 2.3b Vaccine Manufacturers

Between 2005 and 2009, the vaccine industry underwent a period of acquisitions and consolidation. (See Exhibit 10 for a list of acquisitions in the industry.) Companies without vaccine divisions (Novartis, Pfizer) entered the market, and those already established (GSK, Sanofi, Merck) grew larger. By 2013, the vaccine industry was very concentrated, with five multinational firms[n] accounting for over 80% of the market. In 2011, GSK led with 27.4% of the market (and over $5 billion in sales), followed by Sanofi Pasteur with 21.5% and Merck with 19.6%.[24] (See Exhibit 11 for leading global vaccine manufacturers.) The sales of the top-selling vaccine, Prevnar 13 (a vaccine for pneumococcal infection produced by Pfizer), were $1.85 billion in the first half of 2012 alone.[25] (See Exhibit 12 for the top-selling vaccines.)

Vaccine manufacturers balanced profitability with accessibility. The profit margin on vaccines was a third to a half of that of patent-protected drugs,[26] but vaccines experienced smaller revenue and profit falloff after the removal of patent protection. Generic pharmaceutical manufacturers lacked the development capabilities, manufacturing facilities, and capital to produce vaccines, and there was less willingness to outsource the complex production of vaccines to developing markets. As a result, there were few generic vaccine manufacturers. Manufacturing costs as a percentage of sales were higher (44% of revenue versus 24% for pharmaceuticals), but marketing costs were lower than those for patent-protected drugs (16% of revenue versus 29% for pharmaceuticals).[27]

Sales strategies for vaccines in the private segments of developing markets resembled those of pharmaceuticals (large sales force, company reps, etc.). Firms expanding into developing markets used price discrimination to increase sales and overall profitability. (See Exhibit 13 for

n The five firms were Sanofi Pasteur, GlaxoSmithKline (GSK), Merck, Pfizer, and Novartis.

## EXHIBIT 10 Vaccine-Related Acquisitions, 2005–2009

| Target Company | Acquiring Company | Investment ($) | Date Announced |
|---|---|---|---|
| Crucell | Johnson & Johnson | $ 2.6 billion | Sep 2009 |
| Shantha Bio | Sanofi | 781 million | July 2009 |
| Wyeth | Pfizer | 68 billion | Jan 2009 |
| Acambis | Sanofi | 549 million | July 2008 |
| Coley | Pfizer | 214 million | Nov 2007 |
| Intercell | Novartis | 363 million | July 2007 |
| MedImmune | AstraZeneca | 15.6 billion | April 2007 |
| PowderMed | Pfizer | 230 million | Oct 2006 |
| Chiron | Novartis | 5.1 billion | Oct 2005 |
| ID Biomedical | GSK | 1.4 billion | Sep 2005 |
| Corixa | GSK | 300 million | May 2005 |

*Source: Adapted from Miloud Kaddar, "Global Vaccine Market Features and Trends," World Health Organization presentation, 2012, http://who.int/influenza_vaccines_plan/resources/session_10_kaddar.pdf, accessed January 2014*

## EXHIBIT 11 Top Global Vaccine Manufacturers, 2012

| Company | Market Share[a] | Vaccine Sales |
|---|---|---|
| Sanofi[b] | 23.1% | $5.54 billion |
| Merck | 22.0% | $5.27 billion |
| GSK | 21.9% | $5.26 billion |
| Pfizer | 17.1% | $4.11 billion |
| Novartis | 5.8% | $1.38 billion |

*Source: Adapted from Miloud Kaddar, "Global Vaccine Market Features and Trends," World Health Organization presentation, 2012, http://who.int/influenza_vaccines_plan/resources/session_10_kaddar.pdf, accessed January 2014*

[a] Casewriter estimates using estimated total vaccine market size for 2012 of $24 billion.

[b] Sanofi MSD was a joint venture between Sanofi and Merck. Each participant owned 50% of the firm. The joint venture itself partnered with Sanofi in some cases (hence Sanofi and Sanofi MSD).

## EXHIBIT 12 Top-Selling Vaccines, 2012

| Vaccine Name | Manufacturer | Type | 2012 Sales[a] |
|---|---|---|---|
| Prevnar 13 | Pfizer | Pneumococcal conjugate | $3.7 billion |
| Gardasil | Merck & Sanofi MSD[b] | Human papillomavirus | $1.9 billion |
| PENTAct-HIB | Sanofi & Sanofi MSD | Hib, tetanus, diphtheria, polio, and pertussis | $1.5 billion |
| Infanrix/Pediarix | GSK | Hepatitis B, tetanus, diphtheria, polio, & pertussis | $1.2 billion |
| Fluzone | Sanofi & Sanofi MSD | Influenza | $1.2 billion |
| Hepatitis franchise | GSK | Hepatitis A & B | $986 million |
| Varivax | Merck & Sanofi MSD | Varicella | $846 million |
| Menactra | Sanofi & Sanofi MSD | Meningococcal and diphtheria | $735 million |
| Zostavax | Merck & Sanofi MSD | Zoster | $651 million |
| Rotateq | Merck & Sanofi MSD | Rotavirus | $648 million |

*Source: Adapted from "Top 15 Vaccines of 2012," Genetic Engineering and Biotechnology News, http://www.genengnews. com/insight-and-intelligenceand153/top-15-vaccines-of-2012/77899844/?page=1, accessed January 2014.*

[a] Casewriter estimates using estimated total vaccine market size for 2012 of $24 billion.

[b] Sanofi MSD was a joint venture between Sanofi and Merck. Each participant owned 50% of the firm. The joint venture itself partnered with Sanofi in some cases (hence Sanofi and Sanofi MSD).

vaccine revenue and population by region.) The importance of manufacturers based in emerging markets was growing thanks to lower cost structures and increasing participation (49% of pre-qualified vaccines were created by emerging market manufacturers[o] in 2010).[28] (See Exhibit 14 for the growth of pre-qualified vaccines by emerging market manufacturers.)

### 2.3c Vaccine Customers and Consumers

The main customer groups that purchased vaccines were governments (to supply inoculations to the public) and travelers (who often paid for vaccines out of pocket). The majority of vaccines were sold to governments and international organizations; these commanded lower prices than those sold in the private sector.

## 2.4 International Organizations

The Bill and Melinda Gates Foundation was the largest private foundation in the world and comprised three grant-providing subdivisions: the Global Health Program, the Global Development Program, and the United States Program.[29] The Global Health Program provided funding to numerous programs dedicated to increasing immunization, including: GAVI (the Global Alliance for Vaccines and Immunization); the Global Polio Eradication Initiative; and a number of product development partnerships such as the Malaria Vaccine Initiative, the Aeras Global TB Vaccine Foundation, and the Neglected Tropical Diseases Initiative.

The Pan American Health Organization (PAHO) was the regional office of the World Health Organization (WHO) and served the Americas. Founded in 1902, PAHO was the oldest international public health agency worldwide. Through its revolving fund, PAHO/WHO offered a cooperative purchasing mechanism for vaccines, which were then distributed throughout the Americas. In 2012, the fund procured over 200 million doses for 28 different vaccines at a cost of $518 million.[30]

Established in 2000, GAVI was an international public-private partnership dedicated to increasing global immunization rates. GAVI's donors included the WHO, UNICEF, the World Bank, and the Bill and Melinda Gates Foundation. Due to its size, GAVI was able to negotiate low prices for vaccines supplied to developing nations: in 2012, GAVI was able to supply

o Takeda was not included on the list of emerging manufacturers.

## EXHIBIT 13 Vaccine Revenue and Population by Region, 2013

| | Vaccine Sales ($, million) | % of Global Vaccine Sales | % of Global Population |
|---|---|---|---|
| United States | $3,555 | 34.4% | 4.4% |
| North America[a] | $330 | 3.2% | 4.4% |
| South America | $703 | 6.8% | 4.6% |
| Europe | $3,162 | 30.6% | 10.5% |
| Japan | $806 | 7.8% | 1.8% |
| India | $682 | 6.6% | 17.1% |
| China | $785 | 7.6% | 19.0% |
| Other | $310 | 3.0% | 38.2% |

*Source: Adapted from Alison Sahoo, "Vaccines 2012," Kalorama Information Market Intelligence Report, September 2012, p. 145, via Marketresearch.com, accessed January 2014; U.S. Census Bureau, "International Data Base," December 2013, http://www.census.gov/population/international/data/idb/informationGateway.php, accessed January 2014.*

[a] Including the Caribbean; excluding the United States.

## EXHIBIT 14 Pre-Qualified Vaccines by Emerging Market Manufacturers, 2003–2010

| Year | Total Pre-Qualified Vaccines | Pre-Qualified by Emerging Market Mfrs. | % of Pre-Qualified by Emerging Market Mfrs. | Emerging Mfr. Countries with Functional NRAsa |
|---|---|---|---|---|
| 2003 | 66 | 21 | 32% | 6 |
| 2006 | 73 | 31 | 43% | 6 |
| 2009 | 98 | 47 | 48% | 6 |
| 2010 | 102 | 50 | 49% | 7 |

*Source: Adapted from Miloud Kaddar, "Global Vaccine Market Features and Trends," World Health Organization presentation, 2012, http://who.int/influenza_vaccines_plan/resources/session_10_kaddar.pdf, accessed January 2014.*

[a]National regulatory authorities.

the human papillomavirus (HPV)[p] vaccine, Gardasil, at $5 per dose in developing markets, while the cost of a dose was roughly $150 in the United States.[31] By 2014, GAVI had promised over $8.4 billion in vaccine funding through 2016 to the world's poorest countries.[32]

UNICEF was the world's largest buyer and supplier of vaccines for developing countries and served as the procurement agent for GAVI. UNICEF partnered with manufacturers to obtain vaccines at affordable prices (which ultimately reached 36% of the world's children).[33] In 2012, UNICEF purchased about 50% of global vaccine volume (in doses) sold but accounted for only about 5% of the total vaccine sales in dollar terms.[34] In 2009, UNICEF procured all vaccines for GAVI's programs at a cost of $390 million.[35] In 2011, UNICEF and PAHO procured $1.43 billion of vaccines, or roughly 7.5% of total vaccines sold by value (an increase of over fivefold since 2000).[36] The growth was driven by the scaling of campaigns, new vaccines, price increases, the emphasis on eradicating polio, and the creation of GAVI.[37]

In the U.S., volume discounts for vaccines purchased by the government resulted in prices that

p Human papillomavirus (HPV) was a sexually transmitted infection that caused health problems such as genital warts, recurrent respiratory papillomatosis (throat warts), and cervical cancer.

were 30% to 60% lower than in the private sector.[38] "Blockbuster vaccines" and new, specialized vaccines commanded smaller discounts.[39] (See Exhibit 15 for private sector versus public sector vaccine prices.) A dose of flu vaccine, for example, sold to a government health agency for $3.30 in 2013,[40] while a dose sold to a pharmacy chain for $15 might then be sold directly to the consumer at an in-store clinic for $30.[41]

## 2.4a Vaccinations in Developing Markets

The world's poorest regions suffered disproportionately from infectious diseases. According to the WHO, infectious diseases were responsible for one-third of all deaths in 2012, killing at least 15 million people and contributing significantly to the life expectancy disparity between rich and poor countries (average life spans of 77 versus 52 years, respectively).[42] At least 2 million children died each year from diseases that were preventable using existing vaccines.[43] Many more suffered disability and illness as a result of low vaccination rates.

Developing nations suffered greater shortages of all types of medicines, including vaccines, than developed markets. This was in part due to the limited ability of individuals and governments in these markets to pay the same prices as developed countries for vaccines. Typically, there had been up to a 15- to 20-year gap between the launch of a new vaccine in developed countries and distribution in poorer countries, mainly due to high costs of commercializing new vaccines (reaching $500 million and greater) and the need for vaccine manufacturers to recoup their research and development investment.[44]

Barriers to distribution were another contributing factor to the difficulty of obtaining vaccines in developing nations.[q] Almost all vaccines had to be refrigerated or frozen throughout the supply chain in order to maintain their efficacy.[45] As a result, a cold chain system was necessary for the storage and transportation of vaccines. However, such systems were often incomplete, required maintenance, and suffered vaccine waste rates of up to 50%, especially in emerging markets.[46]

q Even new vaccines that had higher heat tolerances were often transported via cold chain systems until their stability was verified.

**EXHIBIT 15 Vaccine Prices for Private Sector versus Public Sector for Selected Vaccines, 2012**

| Vaccine | Manufacturer | Vaccine Type | Private Sector Price | Public Sector Price |
|---|---|---|---|---|
| ActHIB | Sanofi | Haemophilus influenzae type B | $25.47 | $9.00 |
| Havrix | GSK | DtaP | $28.74 | $14.25 |
| Tripedia | Sanofi | Hepatitis B | $26.38 | $13.25 |
| Fluarix | GSK | Influenza | $10.28 | $8.90 |
| FluMist | AstraZeneca | Influenza | $19.70 | $15.70 |
| Twinrix | GSK | Hep A Adult | $92.50 | $43.48 |
| Afluria | CSL Limited | Influenza | $10.25 | $8.25 |
| Decavac | Sanofi | Tetanus & Diphtheria | $21.15 | $16.50 |
| MMRII | Merck | Measles, Mumps, Rubella | $50.16 | $35.77 |
| Zostavax | Merck | Zoster Vaccine | $83.70 | $69.73 |
| ENGERIXB | GSK | Hepatitis B | $52.50 | $27.33 |
| Cervavix | GSK | HPV | $128.75 | $96.08 |
| Gardasil | Merck | HPV | $130.27 | $95.27 |
| Prevnar | Pfizer | Pneumococcal | $120.85 | $97.21 |

*Source: Adapted from Jon Evans, "Vaccine Production," Kalorama Information Market Intelligence Report, February 2012, p. 33, via Marketresearch.com, accessed January 2014.*

# 2.5 Takeda's Vaccine Strategy

## 2.5a Domestic Vaccine Business

Takeda had sold vaccines in Japan since 1946. In 2013, Takeda was the fifth largest vaccine manufacturer in Japan, with 12.1% of the market by value. Takeda's domestic portfolio comprised nine vaccines (listed in order of FY2012 revenues):

- Measles-rubella combined vaccine
- Influenza vaccine
- Japanese encephalitis vaccine
- Diphtheria-pertussis-tetanus combined vaccine
- Mumps vaccine
- Rubella vaccine
- Diphtheria-tetanus combined toxoid
- Tetanus toxoid
- Measles vaccine

Two of its vaccines, the influenza vaccine and the measles/rubella combination, were among the top 10 vaccines sold in Japan, and between them brought in 16.8 billion yen (based on the suggested retail price) in 2013.

When asked about the future of Takeda's domestic vaccine business, Dr. Masato Iwasaki, the company's director and senior vice president, Pharmaceutical Marketing Division, stated:

> *We will further enhance our over 60-years-old domestic vaccine business and forge even stronger partnerships with our affiliates and wholesalers. All these activities will lead us to maintain our share in the Japanese vaccine market.*

Takeda collaborated closely with the Japanese government to craft strategies to combat the threat of influenza pandemics. In 2009, the WHO issued a Phase 5 alert on the H1N1, or "swine flu," virus, which indicated that the virus had spread to two or more countries and risked causing large outbreaks. (It was the first time a virus had been classified as Phase 5.)[47] The Japanese government had not stockpiled enough vaccine doses for its population and was forced to bid for vaccines on the global market. In 2011, following the swine flu outbreak, the government of Japan provided Takeda with a subsidy of 23.9 billion yen to fund the expansion of its influenza vaccine production capacity, with the understanding that Takeda would provide essential vaccines to the Japanese health ministry for no profit.

Takeda pursued partnerships to broaden its vaccine portfolio in Japan. In 2009, Takeda and Novartis reached an agreement to distribute Vaxem-Hib[r] in Japan. Novartis manufactured the vaccine, and Takeda took responsibility for conducting clinical trials and submitting applications to obtain the right to license, market, and distribute the vaccine in Japan under the Takeda brand name.[48] In 2010, Takeda entered an agreement with Baxter to jointly develop and license an H5N1 pandemic influenza vaccine in Japan.[49] In 2012, Takeda's vaccine division was working on vaccines for HPV, polio, and Hib. The firm submitted a new drug application to the Japanese Ministry of Health, Labour and Welfare for the Hib vaccine (licensed from Novartis) for use in Japan.[50] In the same year, the firm entered into a three-year agreement with Osaka University to establish a Joint Research Chair to develop nanoparticle vaccines, which delivered vaccine doses to mucosal surfaces in the lungs, gastrointestinal tract, and reproductive tract. Furthermore, Takeda commenced the sale of a freeze-dried, live, attenuated varicella vaccine created by the Research Foundation for Microbial Diseases of Osaka University in February 2014.

But the growth of the vaccine market in Japan was slow: in 2011, Japan accounted for 7.9% ($1.5 billion) of global vaccine sales, but its growth rate was expected to trail the world average (8.7% annual growth), resulting in 2016 sales of only $2.3 billion.[51]

## 2.5b Global Vaccine Strategy

The threat of the impending patent cliff and Hasegawa's desire to expand globally in a sustainable manner helped to guide Takeda's decision to expand its domestic vaccine business. Initially, vaccines were seen as a stable portfolio option, as they carried lower risks and rewards than drugs (which had higher rates of failure during trials and were subject to patent cliffs). Dr. Iwasaki observed, "The cost of Phase I clinical trials for vaccines is high; however, if a vaccine passes Stage I, its probability of successfully reaching the market is much higher than that of a drug that had passed Phase I." Additionally, vaccines allowed the company to reach

r Haemophilus influenzae type b (Hib) was an "invasive disease" that infected areas of the body normally spared from germs, such as blood. Spread via contact with infected mucus or saliva, Hib could lead to meningitis, pneumonia, and epiglottitis (restricted airways due to swelling of the throat).

a broader range of people, providing a natural extension beyond the company's existing roles in treatment and alleviation and expanding the company's operations into preventive treatments. Vaccines were paramount in developing markets where the broader pharmaceutical industry was still growing. Successful entry into a country's vaccine supply chain could later be leveraged to expand Takeda's sales of pharmaceuticals as the country and its healthcare system developed.

Dr. Yamada played a key role in confirming vaccines as a strategic focus for the company. He drew from his prior experience working at the Bill and Melinda Gates Foundation and at GSK to share the following principles for bringing development projects from the lab to commercial reality:

- **Personalize a Sense of Urgency:** At the end of every action undertaken by the foundation was a sick patient. Field experience was invaluable in motivating this sense of urgency.
- **Innovation:** An impetus was needed to create what was revolutionary versus evolutionary.
- **Partnerships:** "If you want to go fast, walk alone. If you want to go far, walk together."
- **Measurement:** "If you're not keeping score, you're just practicing."

Dr. Yamada's experience contributed to Takeda the confidence that it needed to set the high goal of becoming the first Japanese company to be one of the top five global manufacturers of vaccines, and under his direction Takeda began to acquire companies with strong vaccine pipelines.

In January 2012, Takeda created the Vaccine Business Division in order to globalize its approximately 20 billion yen vaccine business, which at the time was entirely domestic and accounted for only 1.5% of Takeda's total revenues. The division was headed by Dr. Rajeev Venkayya, the former director of vaccine delivery in the Global Health Program at the Bill and Melinda Gates Foundation. The division employed around 230 people, and research sites dedicated to vaccines obtained through acquisitions proved key to this effort. The existing domestic vaccine portfolio included no distinctive products that would warrant an international sales effort. Moreover, Takeda did not have vaccines in its pipeline, nor did it have funding to develop additional vaccine candidates internally from scratch. Because of this, the division focused on acquiring or licensing mid- to late-stage vaccine candidates to sell worldwide. The vaccine division also pursued the development of technology platforms to further expand its pipeline.

A key element of Takeda's vaccine strategy was to invest in companies with strong vaccine pipelines and top talent. Takeda acquired LigoCyte Pharmaceuticals in October 2012. LigoCyte was a U.S. biotechnology firm specializing in the development of vaccines using a proprietary virus-like particle (VLP). VLP technology was used in the HPV and hepatitis B vaccines. LigoCyte was using its VLP platform to develop a norovirus vaccine (to address gastroenteritis, which impacted 21 million people in the U.S. and over 267 million worldwide in 2012).[52] In May 2013, Takeda acquired Inviragen, a biotechnology firm specializing in viral vaccines. Inviragen's portfolio included vaccines in development for dengue fever (which impacted over 300 million people each year worldwide); enterovirus-71 (EV-71, a major cause of hand, foot, and mouth disease); and chikungunya.[s]

Through the acquisition of LigoCyte, Takeda obtained the only late-stage norovirus vaccine in the world. The norovirus vaccine's VLP technology mimicked the "shell" of the virus, leading the body to respond as it would to norovirus, without carrying any of the genetic material of the real virus. Two studies showed that the vaccine was capable of preventing infections from genogroup I and genogroup II noroviruses (two very common viruses causing norovirus infections). The prospective market for the norovirus vaccine was thought to be broader than children alone: institutions such as restaurants, hospitals, schools, day care centers, and cruise lines had a vested interest in encouraging immunizations for their staff and customers to prevent costly norovirus outbreaks.

Dengue infections were caused by one of four viruses: dengue type 1 (DEN-1), DEN-2, DEN-3, and DEN-4. The dengue vaccine Takeda acquired from Inviragen contained four vaccine strains to protect against all dengue virus types. Clinical testing of the dengue vaccine found it generated immune responses to the virus.[53] Sanofi Pasteur also possessed a late-stage dengue vaccine that was slated for release in 2015. As a result, Takeda's dengue vaccine would likely be second to market.

Acknowledging that dengue fever impacted both rich and poor, Takeda expected to adopt a tiered pricing system for its vaccines, collecting higher prices and margins in wealthier countries and lower prices and

s Chikungunya was a viral disease transmitted by mosquitos.

margins (but with greater accessibility) in poorer countries. Many existing vaccine players waited three to five years before launching vaccines in poorer countries (at lower prices). At Takeda, Dr. Venkayya's goal was to launch vaccines in wealthy and poor countries simultaneously. "We are not going to lose money in poor markets—this is not sustainable," he said. We are going to drive our costs down so we can break even in poor countries and meet internal return on investment hurdles." Unlike other pharmaceuticals, the expiration of patents on vaccines seldom impacted sales (making investments in vaccine development more sustainable than other types of pharmaceuticals).

Competition in the vaccine industry was not as intense as in the broader pharmaceuticals category, so Takeda saw an opportunity to move into a leadership position via the creation of one or two blockbuster vaccines. Dr. Venkayya carefully selected vaccine projects according to the following criteria: greatest expected impact on global public health, commercial attractiveness, likely time to market, the competitive landscape, and the probability of clinical success. The top five vaccine companies each owned at least one "blockbuster" vaccine with over $1 billion in annual sales. Given the expected time to market of Takeda's pipeline vaccines, Dr. Venkayya anticipated that the company would have at least one blockbuster vaccine by 2020. (See Exhibit 16 for Takeda's vaccine pipeline.)

Some observers believed that Takeda could succeed in vaccines if the correct targets were set. There were many opportunities for vaccines to grow: particularly in targeting prophylactic vaccines for diseases for which there were no vaccines previously and therapeutic vaccines designed to prevent cancer and other types of illness. However, success in vaccines required at least a five-year investment. For example, the development of Pfizer's blockbuster vaccine, Prevnar, required several hundred million dollars invested in research and development and 12 years to bring to market.

The development process for prophylactic vaccines required substantial investments in clinical development, including a large prevention trial (potentially with over 20,000 participants) and postmarketing studies in much larger populations, typically to ensure product safety. Global reach was required to achieve the scale needed to justify investment in the trials. In the case of vaccines for diseases of developing countries, external support from funders such as foundations and governments, long-term commitments through GAVI, and mechanisms such as advance market commitments (AMC) were often needed to successfully bring a new vaccine to market. (AMCs often carried specified pricing and supply requirements, and design specifications requested by experts in the target regions.)[54] The development timeline from bench to market for vaccines was comparable to that for drugs.

Dr. Venkayya anticipated operational challenges in building a global vaccine business. Takeda needed to extend its vaccine marketing reach outside of Japan and develop capacity to sell in private and public markets around the world. This included marketing vaccines to global procurement entities such as GAVI and PAHO. Expanding the business would require a global manufacturing footprint that would be built upon the capacity of Takeda's Hikari plant in Japan. As a newcomer to the global vaccine arena, Takeda had relative flexibility in its decisions regarding its manufacturing and commercialization strategies. Dr. Venkayya was committed to lowering manufacturing costs to lower prices and improve access to vaccines among poor people. His plans included several key innovations: modular, smaller manufacturing equipment that could be installed in any building; disposable equipment that would not require meticulous and costly cleaning; and process improvements to boost the yield of existing

## EXHIBIT 16 Takeda's Vaccine Pipeline (Phase II or Beyond), 2013

| Development Code | Type | Distribution |
|---|---|---|
| BLB-750 | Influenza | Domestic |
| TAK-816 | Hib | Domestic |
| TAK-361S | Diphtheria, tetanus, polio & pertussis | Domestic |
| Norovirus vaccine | Norovirus | International |
| DENVax | Dengue fever | International |

*Source: Company documents*

production processes. Sales of vaccines outside of Japan were expected to commence in 2017.

Under Takeda's normal budgeting process, funding for global vaccine investments would come from profits on domestic vaccine sales. However, since domestic vaccine profits were insufficient, cross-subsidization from Takeda corporate was deemed necessary for the first four years. (Roughly 4% of Takeda's 2013 budget was allocated to vaccines, domestic and international.)[55] Despite the potential for success, Dr. Venkayya and his team faced a degree of internal skepticism that the vaccine business would not be financially successful. Some at Takeda viewed the vaccine strategy as a corporate social responsibility project and wondered what an "ethical" profit on vaccines could be.

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