

(4) Risk Factors in Business

Takeda's business performance is exposed to various risks at present and in the future, and may experience unexpected fluctuations due to occurrence of those risks. The below is a discussion of assumed main risks Takeda might face in its business activities. Takeda intends to work to prevent such occurrence, insofar as possible—while fully identifying these potential risks—and will ensure a precise response in the event of their occurrence.

In addition, the future events contained in these items are envisioned as of the end of this fiscal term.

1. Risks in R&D

While Takeda strives for efficient R&D activities aimed at launching new products in the trilateral markets of Japan, U.S. and Europe as early as possible, ethical drugs are in nature only allowed placement on the market when they are approved through rigorous investigations of efficacy and safety as stipulated by the competent authorities, irrespective of in-house or licensed compounds.

If it turns out that the efficacy and safety of such compounds do not meet the required level for approval, or if reviewing authorities express concern regarding the nonconformity of such compounds, Takeda will have to give up R&D activities for such compounds at that point, or will conduct additional clinical or non-clinical testing. As a result, Takeda might be exposed to risk of uncollectibility of costs incurred, experience delay in launching new products, or be forced to revise its R&D strategy.

2. Risk in intellectual property rights

Takeda's products are protected by two or more patents covering substance, processes, formulations and uses for a certain period.

While Takeda strictly manages intellectual property rights, including patents, and always keeps careful watch for potential infringement by a third party, expected earnings may be lost if the intellectual property rights held by Takeda are infringed by a third party. Moreover, if Takeda's in-house product proves to infringe a third party's intellectual property rights, Takeda might be asked for compensation.

3. Risk in sales decrease following patent expirations

While Takeda takes active measures to extend product life-cycles, including the addition of new indications and formulations, generic drugs inevitably penetrate the market following patent expirations of most of branded products. In addition, as the increasing use of generic drugs and prescription-to-OTC switches also intensifies competition, both in domestic and overseas markets, especially in the U.S. market, Takeda's sales of ethical drugs may drop sharply, depending on influences.

4. Risk in side effects

Although ethical drugs are only allowed placement on the market after approval for production and marketing following rigorous investigation by the competent authorities around the world, accumulated data during the post-marketing period might expose side effects not confirmed at launch. If new side effects are identified, Takeda will be required to describe such side effects in a "precautions" of the package insert or to restrict usage of such drugs, or will be forced to discontinue sale of or recall such products.

5. Risk in price-lowering due to measures for reducing drug prices

In the United States market, which is the world's largest, federal and state governments, as well as private insurance companies, implement various measures to reduce drug costs, further

increasing the pressure to reduce prices of branded products. In Japan, National Health Insurance (NHI) prices for drugs have been reduced every other year. In the European market, drug prices have been reduced in a similar way, due to strong measures to control drug costs in each country, and the expansion of parallel imports. Price reduction as a result of drug cost-restrictive measures taken by each country can significantly influence the business performance and financial standing of Takeda Group.

6. Influence from exchange fluctuations

Takeda Group's overseas net sales in this fiscal term amounted to ¥ 478.4 billion, which accounted for 42.6% of total consolidated sales. Among others, sales in North America were ¥ 287.4 billion, which accounted for 25.6% of total consolidated sales. Moreover, with regard to TAP, the "equity in earnings of affiliates" (non-operating income) was ¥ 40.3 billion. For this reason, Takeda Group's business performance and financial standings are considerably affected by currency rates, especially fluctuations in the dollar-yen conversion rate.

7. Risk in development of lawsuits

Civil litigations by patients and insurance companies etc. seeking damages (sometimes called 'AWP Suit'), which involve numerous major U.S. pharmaceutical companies, are currently under disputation on an industry-wide scale. The complaints claim damages due to price discrepancies between the AWP (Average Wholesale Prices) as made publicized by independent industry compendia and the actual selling prices. As part of the civil litigations, actions have been brought against TAP and TPNA for damages in federal and state courts; Takeda has also faced part of such litigations. The progress of these suits may affect Takeda's business performance and financial standing.

If Takeda's main products, *Leuplin*, *Lansoprazole*, *Candesartan* and *Actos*, are involved in the above risk occurrence, Takeda's business performance might be greatly affected.