Better Health, Brighter Future

# Financial Results for FY2013

# DATA BOOK


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**Quarterly Announcements / Presentations**
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## Takeda-ism

We, the members of the Takeda Group, pledge to act with integrity at all times, especially when facing difficulties or challenges. "Integrity" refers to our compliance with the highest ethical standards, our fairness and honesty in conducting every activity, and our perseverance in pursuing the ideal forms for our operations and management. Through the demonstration of these qualities, we show our commitment to building trust and confidence in all the people around us, and our determination to continue to expand the business. These empower our progress in our global endeavors to fulfill our mission to "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.

- **Our Business: Committed to Improving Health**

  With countless people in desperate need of new healthcare solutions, there's no time to wait. That's why we pursue innovative medicines as well as high-quality branded generics, life-saving vaccines, and OTC medicines – to help as many people as we can, as soon as we can.

- **Our Organization: Strength from Diversity**

  A common set of values, Takeda-ism, unites us as one. Using our diverse skills and ideas, we develop fresh solutions to meet the needs of people around the world. Each one of us is empowered to act swiftly and decisively in our quest to improve quality of life.

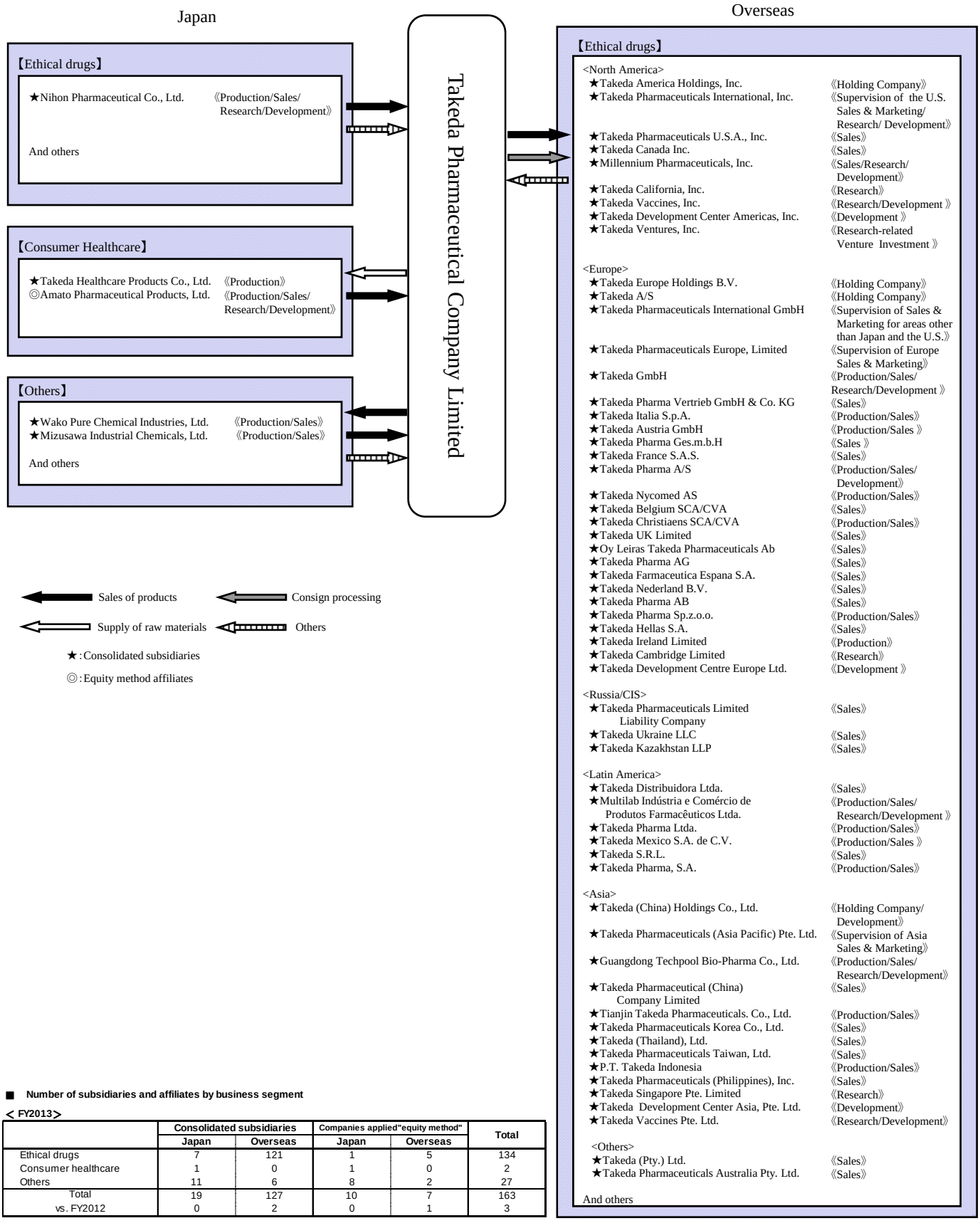
- **Our People: Powered by Passion**

  Our people are our greatest asset. Driven by passion to learn and contribute more, we embrace new challenges with confidence and open minds. We are determined to lead the change for a better world.

## Contents

# I. Overview of Takeda group

The Takeda Group consists of 164 companies, including the parent company submitting these consolidated financial statements, 146 consolidated subsidiaries and 17 affiliates accounted for by the equity method. The following chart shows the main business areas of the Takeda Group, the position of the companies that make up the Group within their respective areas of business, and relationships with each business segment.




■ **Number of subsidiaries and affiliates by business segment**

**＜FY2013＞**

| | Consolidated subsidiaries | | Companies applied"equity method" | | Total |
|---|---|---|---|---|---|
| | Japan | Overseas | Japan | Overseas | |
| Ethical drugs | 7 | 121 | 1 | 5 | 134 |
| Consumer healthcare | 1 | 0 | 1 | 0 | 2 |
| Others | 11 | 6 | 8 | 2 | 27 |
| Total | 19 | 127 | 10 | 7 | 163 |
| vs. FY2012 | 0 | 2 | 0 | 1 | 3 |

## II. Financial highlights (IFRS) **(more detail will be available in Page 4 and onward)**

| **Consolidated Operating Results (Billions of Yen)** | FY12 (IFRS) | **FY13 (IFRS)** | vs. FY12 | increase/ decrease | **FY14 Estimate (IFRS)** | FY14 1st half |
|---|---|---|---|---|---|---|
| Revenue | 1,557.0 | **1,691.7** | 134.7 | 8.6% | **1,725.0** | 845.0 |
| Overseas Revenue | 822.7 | **957.8** | 135.1 | 16.4% | **1,005.0** | 486.0 |
| <% of Revenue> | <52.8%> | **<56.6%>** | <3.8pt> | | **<58.3%>** | <57.5%> |
| Revenue of Ethical drugs segment | 1,401.5 | **1,529.1** | 127.5 | 9.1% | **1,564.0** | 766.0 |
| R&D Expenses | 321.3 | **341.6** | 20.2 | 6.3% | **350.0** | 160.0 |
| <% of Revenue> | <20.6%> | **<20.2%>** | <-0.4pt> | | **<20.3%>** | <18.9%> |
| Operating Profit | 65.0 | **139.3** | 74.3 | 114.3% | **150.0** | 90.0 |
| <% of Revenue> | <4.2%> | **<8.2%>** | <4.1pt> | | **<8.7%>** | <10.7%> |
| Profit before income taxes | 133.1 | **158.9** | 25.8 | 19.4% | **140.0** | 85.0 |
| <% of Revenue> | <8.5%> | **<9.4%>** | <0.8pt> | | **<8.1%>** | <10.1%> |
| Net profit for the year | 150.7 | **109.6** | -41.1 | -27.3% | | |
| <% of Revenue> | <9.7%> | **<6.5%>** | <-3.2pt> | | | |
| Profit attributable to owners of the Company | 148.6 | **106.7** | -41.9 | -28.2% | **85.0** | 50.0 |
| <% of Revenue> | <9.5%> | **<6.3%>** | <-3.2pt> | | **<4.9%>** | <5.9%> |
| Core Earnings * | 285.5 | **314.2** | 28.7 | 10.1% | **280.0** | 145.0 |
| <% of Revenue> | <18.3%> | **<18.6%>** | <0.2pt> | | **<16.2%>** | <17.2%> |

* Profit from regular business calculated by deducting any temporary factors such as impacts from business combination accounting and from amortization/impairment loss of intangible assets etc., from operating profit.

| **Consolidated Financial Position (Billions of Yen)** | FY12 End (IFRS) | **FY13 End (IFRS)** | vs. FY12 End |
|---|---|---|---|
| Total assets | 4,052.6 | **4,569.1** | 516.6 |
| Total liabilities | 1,714.3 | **2,028.5** | 314.2 |
| Total equity | 2,338.3 | **2,540.6** | 202.3 |
| Equity attributable to owners of the Company | 2,274.1 | **2,470.7** | 196.6 |
| Ratio of equity attributable to owners of the Company to total assets | 56.1% | **54.1%** | -2.0pt |

| **Shares** | FY12 End | **FY13 End** |
|---|---|---|
| Number of shares outstanding (1,000) | 789,666 | **789,681** |
| Treasury Stock（1,000） | 206 | **213** |
| Stock price at year-end (Yen) | 5,030 | **4,892** |
| Total market value (Billions of Yen) | 3,972.0 | **3,863.1** |

| **ROE•EPS•Dividend (Yen)** | FY12 (IFRS) | **FY13 (IFRS)** | vs. FY12 |
|---|---|---|---|
| Return on equity attributable to owners of the Company | 6.8% | **4.5%** | -2.3pt |
| Basic earnings per share | 188.21 | **135.10** | -53.11 |
| Annual dividends per share | 180.00 | **180.00** | - |
| Dividend Pay-out ratio | 95.6% | **133.2%** | 37.6pt |

| **Exchange rate(Yen)** | FY12 | **FY13** | **FY14 Assumptions** |
|---|---|---|---|
| US$ Average (Apr.-Mar.) | 82 | **100** | **100** |
| Euro Average (Apr.-Mar.) | 106 | **133** | **140** |

## <Reference> Financial highlights (J-GAAP)

| **Consolidated Operating Resutls (Billions of Yen)** | FY10 (J-GAAP) | FY11 (J-GAAP) | FY12 (J-GAAP) | FY13 (J-GAAP) | vs. FY12 | increase/ decrease |
|---|---|---|---|---|---|---|
| Net Sales | 1,419.4 | 1,508.9 | 1,557.3 | 1,691.9 | 134.7 | 8.6% |
| Overseas Sales | 698.1 | 775.5 | 822.8 | | | |
| <% of net sales> | <49.2%> | <51.4%> | <52.8%> | | | |
| Net Sales of Ethical drugs segment | 1,267.4 | 1,358.8 | 1,401.7 | | | |
| R&D Expenses | 288.9 | 281.9 | 324.3 | 343.3 | 19.0 | 5.9% |
| <% of net sales> | <20.4%> | <18.7%> | <20.8%> | <20.3%> | <-0.5pt> | |
| Operating Income | 367.1 | 265.0 | 122.5 | 155.7 | 33.2 | 27.1% |
| <% of net sales> | <25.9%> | <17.6%> | <7.9%> | <9.2%> | <1.3pt> | |
| Ordinary Income | 371.6 | 270.3 | 113.2 | 130.7 | 17.5 | 15.5% |
| <% of net sales> | <26.2%> | <17.9%> | <7.3%> | <7.7%> | <0.5pt> | |
| Net Income | 247.9 | 124.2 | 131.2 | 90.3 | -40.9 | -31.2% |
| <% of net sales> | <17.5%> | <8.2%> | <8.4%> | <5.3%> | <-3.1pt> | |
| EBITDA | 484.1 | 422.6 | 323.9 | 381.2 | 57.4 | 17.7% |
| <% of net sales> | <34.1%> | <28.0%> | <20.8%> | <22.5%> | <1.7pt> | |

| **Consolidated Financial Position (Billions of Yen)** | FY10 End (J-GAAP) | FY11 End (J-GAAP) | FY12 End (J-GAAP) | FY13 End (J-GAAP) | vs. FY12 End |
|---|---|---|---|---|---|
| Total assets | 2,786.4 | 3,577.0 | 3,955.6 | 4,374.8 | 419.2 |
| Total liabilities | 649.7 | 1,505.2 | 1,732.2 | 1,986.7 | 254.5 |
| Net assets | 2,136.7 | 2,071.9 | 2,223.4 | 2,388.1 | 164.7 |
| Shareholders' Equity Ratio (%) | 75.1% | 56.2% | 54.6% | 53.0% | -1.6pt |

| **Shares** | FY10 End | FY11 End | FY12 End | FY13 End |
|---|---|---|---|---|
| Number of shares outstanding (1,000) | 789,666 | 789,666 | 789,666 | 789,681 |
| Treasury Stock（1,000） | 295 | 252 | 206 | 213 |
| Stock price at year-end (Yen) | 3,880 | 3,645 | 5,030 | 4,892 |
| Total market value (Billions of Yen) | 3,063.9 | 2,878.3 | 3,972.0 | 3,863.1 |

| **ROE・EPS・Dividend (Yen)** | FY10 (J-GAAP) | FY11 (J-GAAP) | FY12 (J-GAAP) | FY13 (J-GAAP) |
|---|---|---|---|---|
| ROE (Return on equity) | 11.8% | 6.1% | 6.3% | 4.0% |
| EPS (Earnings per share) | 314.01 | 157.29 | 166.25 | 114.44 |
| Annual dividends per share | 180.00 | 180.00 | 180.00 | 180.00 |
| Dividend Pay-out ratio | 57.3% | 114.4% | 108.3% | 157.3% |

| **Exchange rate(Yen)** | FY10 | FY11 | FY12 | FY13 |
|---|---|---|---|---|
| US$ Average（Apr.-Mar.） | 86 | 79 | 82 | 100 |
| Euro Average（Apr.-Mar.） | 113 | 109 | 106 | 133 |

## III. Consolidated Operating Results

### 1. Consolidated Statement of Income (IFRS)

(Billions of Yen)

| | FY12 (IFRS) | **FY13 (IFRS)** | vs. FY12 | increase/ decrease | **Est. FY14 (IFRS)** | Est. FY14 1st half |
|---|---|---|---|---|---|---|
| Revenue | 1,557.0 | **1,691.7** | 134.7 | 8.6% | **1,725.0** | 845.0 |
| Royalty income | 45.2 | **77.4** | 32.2 | 71.3% | | |
| Cost of sales | 463.8 | **490.3** | 26.4 | 5.7% | | |
| <% of revenue> | <29.8%> | **<29.0%>** | <-0.8pt> | | | |
| Gross Profit | 1,093.2 | **1,201.4** | 108.3 | 9.9% | | |
| <% of revenue> | <70.2%> | **<71.0%>** | <0.8pt> | | | |
| SG&A expenses | 512.9 | **556.2** | 43.3 | 8.4% | | |
| <% of revenue> | <32.9%> | **<32.9%>** | <-0.1pt> | | | |
| Advertising and Sales promotion expenses | 86.2 | **105.3** | 19.0 | 22.0% | | |
| Salaries | 119.0 | **133.6** | 14.7 | 12.3% | | |
| Bonuses | 32.1 | **40.7** | 8.6 | 26.7% | | |
| Retirement benefit expenses | 13.2 | **15.4** | 2.2 | 16.5% | | |
| R&D expenses | 321.3 | **341.6** | 20.2 | 6.3% | **350.0** | 160.0 |
| <% of revenue> | <20.6%> | **<20.2%>** | <-0.4pt> | | **<20.3%>** | <18.9%> |
| Amortization and impairment losses on intangible assets associated with products | 173.8 | **143.2** | -30.6 | -17.6% | | |
| Other operating income | 24.1 | **23.9** | -0.3 | -1.1% | | |
| Government grant income | 2.9 | **2.6** | -0.3 | -9.8% | | |
| Rental income | 4.7 | **4.3** | -0.4 | -8.8% | | |
| Gains on sales of property, plant and equipment, intangible assets and investment property | 4.1 | **6.6** | 2.5 | 61.6% | | |
| Royalty income on transfer of operations | 4.3 | **4.7** | 0.4 | 8.7% | | |
| Others | 8.1 | **5.6** | -2.4 | -30.3% | | |
| Other operating expenses | 44.3 | **45.0** | 0.8 | 1.7% | | |
| Expenses directly attributable to rental income | 2.3 | **5.0** | 2.7 | 116.3% | | |
| Donations and contributions | 2.8 | **3.2** | 0.4 | 13.4% | | |
| Restructuring expenses * | 25.2 | **21.7** | -3.6 | -14.1% | | |
| Others | 13.9 | **15.1** | 1.2 | 9.0% | | |
| Operating profit | 65.0 | **139.3** | 74.3 | 114.3% | **150.0** | 90.0 |
| <% of revenue> | <4.2%> | **<8.2%>** | <4.1pt> | | **<8.7%>** | <10.7%> |
| Financial income | 87.7 | **49.3** | -38.4 | -43.8% | | |
| Interest income | 1.2 | **1.4** | 0.1 | 12.2% | | |
| Cash and cash equivalents, loans and other receivables | 1.2 | **1.4** | 0.2 | 12.3% | | |
| Others | 0.0 | **-** | -0.0 | - | | |
| Dividends income | 4.0 | **3.3** | -0.7 | -16.4% | | |
| Gains on sales of available-for-sale financial assets | 56.3 | **40.5** | -15.8 | -28.1% | | |
| Gains on valuation of derivatives | - | **4.1** | 4.1 | - | | |
| Foreign exchange gains | 11.1 | **-** | -11.1 | - | | |
| Interest on tax refund | 15.1 | **-** | -15.1 | - | | |
| Others | 0.1 | **0.0** | -0.0 | -57.1% | | |
| Financial expenses | 20.5 | **30.7** | 10.3 | 50.2% | | |
| Interest expenses | 3.4 | **4.9** | 1.5 | 45.6% | | |
| Fair value adjustments of contingents considerations | 6.5 | **11.0** | 4.5 | 68.4% | | |
| Impairment losses on available-for-sale financial assets | 0.9 | **0.8** | -0.1 | -11.9% | | |
| Losses on valuation of derivatives | 6.7 | **-** | -6.7 | - | | |
| Foreign exchange Losses | - | 11.8 | 11.8 | - | | |
| Others | 2.9 | **2.3** | -0.6 | -21.8% | | |
| Share of profit on investments accounted for using the equity method | 0.9 | **1.0** | 0.1 | 16.1% | | |
| Profit before income taxes | 133.1 | **158.9** | 25.8 | 19.4% | **140.0** | 85.0 |
| Income taxes | -17.6 | **49.3** | 66.9 | - | | |
| Net profit for the year | 150.7 | **109.6** | -41.1 | -27.3% | | |
| <% of revenue> | <9.7%> | **<6.5%>** | <-3.2pt> | | | |
| Attributable to Owners of the Company | 148.6 | **106.7** | -41.9 | -28.2% | **85.0** | 50.0 |
| <% of revenue> | <9.5%> | **<6.3%>** | <-3.2pt> | | **<4.9%>** | <5.9%> |
| Total comprehensive income for the year | 323.3 | **343.7** | 20.4 | 6.3% | | |
| <% of revenue> | <20.8%> | **<20.3%>** | <-0.4pt> | | | |
| Attributable to Owners of the Company | 318.8 | **339.2** | 20.4 | 6.4% | | |
| <% of revenue> | <20.5%> | **<20.0%>** | <-0.4pt> | | | |
| Effective tax rate | | | | | | |
| Japanese statutory tax rate | 38.0% | **38.0%** | - | | | |
| Effective tax rate | △13.2% | **31.0%** | 44.3pt | | | |

* Expenses from reorganization, such as the consolidation of a number of sites and functions (including the potential merger or liquidation of subsidiaries) and the reduction of the workforce to build an efficient operating model. The major item in these expenses was the early retirement payments for the workforce.

**<Reference> Consolidated Statements of Income (J-GAAP)**

(Billions of Yen)

| | FY10 (J-GAAP) | FY11 (J-GAAP) | FY12 (J-GAAP) | FY13 (J-GAAP) | vs. FY12 | increase/ decrease |
|---|---|---|---|---|---|---|
| Net Sales | 1,419.4 | 1,508.9 | 1,557.3 | 1,691.9 | 134.7 | 8.6% |
| Royalty income | 41.4 | 42.5 | 45.2 | 69.3 | 24.1 | 53.4% |
| Cost of sales | 317.6 | 433.2 | 460.7 | 489.0 | 28.3 | 6.1% |
| <% of net sales> | <22.4%> | <28.7%> | <29.6%> | <28.9%> | <-0.7pt> | |
| Gross Profit | 1,101.8 | 1,075.7 | 1,096.6 | 1,202.9 | 106.3 | 9.7% |
| <% of net sales> | <77.6%> | <71.3%> | <70.4%> | <71.1%> | <0.7pt> | |
| SG&A expenses | 734.7 | 810.7 | 974.1 | 1,047.2 | 73.1 | 7.5% |
| <% of net sales> | <51.8%> | <53.7%> | <62.6%> | <61.9%> | <-0.7pt> | |
| SG&A expenses except R&D expenses | 445.8 | 528.8 | 649.8 | 703.9 | 54.1 | 8.3% |
| Selling expenses | 94.5 | 125.2 | 162.5 | 190.9 | 28.4 | 17.5% |
| Advertising expenses | 24.7 | 27.1 | 25.2 | 28.0 | 2.8 | 11.3% |
| Sales promotion expenses | 43.3 | 53.1 | 61.1 | 77.2 | 16.2 | 26.5% |
| Transportation and custody expenses | 8.5 | 11.7 | 16.4 | 17.9 | 1.5 | 9.3% |
| Personnel expenses | 171.8 | 169.4 | 209.6 | 219.1 | 9.4 | 4.5% |
| Other expenses | 179.6 | 234.2 | 277.7 | 293.9 | 16.2 | 5.8% |
| R&D expenses | 288.9 | 281.9 | 324.3 | 343.3 | 19.0 | 5.9% |
| <% of net sales> | <20.4%> | <18.7%> | <20.8%> | <20.3%> | <-0.5pt> | |
| Operating income | 367.1 | 265.0 | 122.5 | 155.7 | 33.2 | 27.1% |
| <% of net sales> | <25.9%> | <17.6%> | <7.9%> | <9.2%> | <1.3pt> | |
| Non-operating income / expenses | 4.5 | 5.3 | -9.3 | -25.1 | -15.7 | 168.4% |
| Total non-operating income | 30.4 | 23.4 | 23.6 | 24.4 | 0.9 | 3.7% |
| Interest income | 1.7 | 1.9 | 1.2 | 1.3 | 0.1 | 9.5% |
| Dividend income | 4.5 | 4.4 | 4.0 | 3.3 | -0.7 | -16.4% |
| Equity in earnings of unconsolidated subsidiaries and affiliates | 0.5 | 0.3 | 0.9 | 1.0 | 0.1 | 13.1% |
| Other non-operating income | 23.8 | 16.8 | 17.5 | 18.8 | 1.3 | 7.3% |
| Total non-operating expenses | 25.9 | 18.1 | 32.9 | 49.5 | 16.6 | 50.4% |
| Interest expenses | 1.3 | 1.9 | 3.3 | 4.5 | 1.1 | 34.2% |
| Loss on inventories | 0.3 | 0.2 | 0.0 | 0.0 | 0.0 | - |
| Loss on marketable securities | 0.3 | 0.1 | 0.8 | 0.0 | -0.8 | -96.4% |
| Loss on fixed assets | 0.9 | 0.7 | 2.6 | 0.6 | -2.0 | -78.1% |
| Contributions | 4.4 | 5.3 | 4.1 | 4.2 | 0.0 | 0.8% |
| Fair value adjustment of contingent consideration | - | - | 6.3 | 11.0 | 4.7 | 75.6% |
| Other non-operating expenses | 18.7 | 9.9 | 15.8 | 29.2 | 13.4 | 85.0% |
| Ordinary income | 371.6 | 270.3 | 113.2 | 130.7 | 17.5 | 15.5% |
| <% of net sales> | <26.2%> | <17.9%> | <7.3%> | <7.7%> | <0.5pt> | |
| Extraordinary income and loss | - | -17.9 | 16.5 | 26.3 | 9.8 | |
| Total extraordinary income | - | 17.6 | 95.0 | 58.9 | -36.1 | -38.0% |
| Gain on sales of investment securities | - | - | 53.1 | 52.2 | -0.9 | -1.7% |
| Gain on sales of noncurrent assets | - | 17.6 | 4.0 | 6.7 | 2.7 | 66.8% |
| Governmental subsidy | - | - | 22.8 | - | -22.8 | - |
| Interest on tax refund | - | - | 15.1 | - | -15.1 | - |
| Total extraordinary loss | - | 35.5 | 78.5 | 32.6 | -45.9 | -58.5% |
| Impairment loss | - | - | 43.6 | 10.9 | -32.7 | -75.0% |
| Restructuring costs | - | 35.5 | 25.2 | 21.7 | -3.6 | -14.1% |
| Loss on voluntary recall of products | - | - | 9.6 | - | -9.6 | - |
| Income before income tax and minority interests | 371.6 | 252.5 | 129.7 | 157.0 | 27.3 | 21.0% |
| Total income taxes | 121.3 | 125.2 | -3.9 | 63.7 | 67.6 | - |
| Minority interests | 2.4 | 3.1 | 2.3 | 2.9 | 0.6 | 24.6% |
| Net income | 247.9 | 124.2 | 131.2 | 90.3 | -40.9 | -31.2% |
| <% of net sales> | <17.5%> | <8.2%> | <8.4%> | <5.3%> | <-3.1pt> | |
| Comprehensive income <incl. minority interests> | 114.5 | 65.4 | 304.1 | 306.1 | 2.0 | 0.7% |
| Effective tax rate | | | | | | |
| Japanese statutory tax rate | 40.9% | 40.6% | 38.0% | 38.0% | - | |
| Effective tax rate | 32.7% | 49.6% | △3.0% | 40.6% | 43.6pt | |

* As for "Royalty" which was included in SG&A expenses in the statement of income under J-GAAP, it is reclassed to Cost of sales in FY12 and FY13 to present the Company's business more adequately after considering the nature of transactions.

## 2. Sales/Revenue

◆ **Sales/Revenue by Regions** (Billions of Yen)

| | FY10 (J-GAAP) | FY11 (J-GAAP) | FY12 (J-GAAP) | FY12 (IFRS) | **FY13 (IFRS)** | vs FY12 | increase/ decrease |
|---|---|---|---|---|---|---|---|
| Total net sales/revenue | 1,419.4 | 1,508.9 | 1,557.3 | 1,557.0 | **1,691.7** | 134.7 | 8.6% |
| Japan | 721.3 | 733.4 | 734.5 | 734.3 | **733.9** | -0.4 | -0.1% |
| Overseas | 698.1 | 775.5 | 822.8 | 822.7 | **957.8** | 135.1 | 16.4% |
| <% of net sales/revenue> | <49.2%> | <51.4%> | <52.8%> | <52.8%> | **<56.6%>** | <3.8pt> | |
| North America and Latin America | 496.4 | | | | | | |
| <% of net sales/revenue> | <35.0%> | | | | | | |
| North America | | 434.2 | 360.6 | 360.5 | **374.5** | 14.0 | 3.9% |
| <% of net sales/revenue> | | <28.8%> | <23.2%> | <23.2%> | **<22.1%>** | <-1.0pt> | |
| [U.S.] | [483.4] | [419.5] | [344.0] | [343.8] | **[352.1]** | [8.2] | [2.4%] |
| Europe and Russia/CIS | 172.9 | | | | | | |
| <% of net sales/revenue> | <12.2%> | | | | | | |
| Europe | | 227.1 | 246.5 | 246.5 | **297.5** | 51.0 | 20.7% |
| <% of net sales/revenue> | | <15.0%> | <15.8%> | <15.8%> | **<17.6%>** | <1.8pt> | |
| Russia/CIS | | 31.0 | 68.3 | 68.3 | **89.6** | 21.2 | 31.1% |
| <% of net sales/revenue> | | <2.1%> | <4.4%> | <4.4%> | **<5.3%>** | <0.9pt> | |
| Latin America | | 30.2 | 62.9 | 62.9 | **81.2** | 18.3 | 29.1% |
| <% of net sales/revenue> | | <2.0%> | <4.0%> | <4.0%> | **<4.8%>** | <0.8pt> | |
| Asia and other | 28.7 | | | | | | |
| <% of net sales/revenue> | <2.0%> | | | | | | |
| Asia | | 38.1 | 60.1 | 60.1 | **85.4** | 25.3 | 42.1% |
| <% of net sales/revenue> | | <2.5%> | <3.9%> | <3.9%> | **<5.0%>** | <1.2pt> | |
| Other | | 15.0 | 24.3 | 24.3 | **29.5** | 5.3 | 21.6% |
| <% of net sales/revenue> | | <1.0%> | <1.6%> | <1.6%> | **<1.7%>** | <0.2pt> | |
| Royalty income | 41.4 | 42.5 | 45.2 | 45.2 | **77.4** | 32.2 | 71.3% |
| Ethical drugs | 41.0 | 42.2 | 44.9 | 44.8 | **77.3** | 32.5 | 72.4% |
| Japan | 0.7 | 0.4 | 0.4 | 0.4 | **0.2** | -0.2 | -46.0% |
| Overseas | 40.3 | 41.8 | 44.5 | 44.4 | **77.1** | 32.7 | 73.5% |

* Sales/Revenue amount is classified into countries or regions based on the customer location.
** Effective from the FY12, the Company changed the classification of region for the purpose of providing more detailed sales/revenue information (previous "Asia and other" was divided into "Asia" and "Other"). At the same time, the regional category of some countries in other than Americas was also changed as this reclassification. In addition, effective from FY13, the Company changed the regional classification for the purpose of clear segmentation between developed countries and emerging markets (previous "Americas" was divided into "North America" and "Latin America" and previous "Europe" was divided into "Europe" and "Russia/CIS"). For fair comparison, the amounts reported in the periods from the FY11 are modified according to the new classification.
*** Other region includes Middle East, Oceania and Africa.

◆ **Ethical Drugs Sales/Revenue** (Billions of Yen)

| | FY10 (J-GAAP) | FY11 (J-GAAP) | FY12 (J-GAAP) | FY12 (IFRS) | **FY13 (IFRS)** | vs FY12 | increase/ decrease |
|---|---|---|---|---|---|---|---|
| Net Sales in Japan | 580.5 | 594.4 | 590.1 | 589.9 | **583.0** | -6.9 | -1.2% |
| Net Sales Overseas | 645.5 | 720.0 | 763.8 | 763.8 | **863.3** | 99.5 | 13.0% |
| North America and Latin America | 475.4 | | | | | | |
| North America | | 417.2 | 343.2 | 343.2 | **340.8** | -2.5 | -0.7% |
| [U.S.] | | [407.3] | [326.8] | [326.8] | **[318.9]** | [-7.9] | [-2.4%] |
| Europe and Russia/CIS | 146.7 | | | | | | |
| Europe | | 194.8 | 211.6 | 211.6 | **243.8** | 32.1 | 15.2% |
| Russia/CIS | | 30.9 | 68.3 | 68.3 | **89.5** | 21.2 | 31.1% |
| Latin America | | 29.9 | 62.3 | 62.3 | **80.6** | 18.3 | 29.4% |
| Asia and other | 23.4 | | | | | | |
| Asia | | 33.6 | 55.5 | 55.5 | **80.5** | 25.1 | 45.2% |
| Other | | 13.6 | 22.9 | 22.9 | **28.1** | 5.2 | 22.7% |
| Royalty income and service income | 44.5 | 47.7 | 50.9 | 50.8 | **85.8** | 35.0 | 68.9% |
| Japan | 1.0 | 1.0 | 1.3 | 1.3 | **2.1** | 0.8 | 66.9% |
| Overseas | 43.5 | 46.6 | 49.5 | 49.5 | **83.7** | 34.2 | 68.9% |
| Total ethical drugs sales/revenue | 1,270.5 | 1,362.0 | 1,404.7 | 1,404.5 | **1,532.1** | 127.6 | 9.1% |
| Ratio of overseas ethical drugs sales/revenue | 54.2% | 56.3% | 57.9% | 57.9% | **61.8%** | 3.9pt | |

* Sales/Revenue amount is classified into countries or regions based on the customer location.
** Sales/Revenue amount includes intersegment sales.
*** Effective from the FY12, the Company changed the classification of region for the purpose of providing more detailed sales/revenue information (previous "Asia and other" was divided into "Asia" and "Other"). At the same time, the regional category of some countries in other than Americas was also changed as this reclassification. In addition, effective from FY13, the Company changed the regional classification for the purpose of clear segmentation between developed countries and emerging markets (previous "Americas" was divided into "North America" and "Latin America" and previous "Europe" was divided into "Europe" and "Russia/CIS"). For fair comparison, the amounts reported in the periods from the FY11 are modified according to the new classification.
**** Other region includes Middle East, Oceania and Africa.

◆ **Subsidiaries and Affiliates *** (Billions of Yen)

| | FY10 | FY11 | FY12 | **FY13** | vs FY12 | increase/ decrease |
|---|---|---|---|---|---|---|
| Takeda Pharmaceuticals U.S.A., Inc. | 400.2 | 328.5 | 234.9 | **213.0** | -21.9 | -9.3% |
| [Millions of US$] | [4,668] | [4,154] | [2,856] | **[2,126]** | [-730] | [-25.6%] |
| Millennium Pharmaceuticals, Inc. | 74.7 | 87.3 | 108.4 | **144.3** | 35.9 | 33.1% |
| [Millions of US$] | [872] | [1,104] | [1,318] | **[1,440]** | [123] | [9.3%] |
| Wako Pure Chemical Industries, Ltd. | 70.0 | 60.2 | 60.3 | **60.8** | 0.5 | 0.9% |

* Sales amounts for TPC group's intercompany transaction are subtracted.

◆ **Ethical Drugs: Global major products' sales**

(Billions of Yen)

| Product | FY10 | FY11 | FY12 | **FY13** | vs. FY12 | increase/ decrease | **FY14 Estimate** |
|---|---|---|---|---|---|---|---|
| Candesartan | 218.0 | 216.3 | 169.6 | **155.0** | -14.6 | -8.6% | **120.0** |
| Leuprorelin | 116.4 | 120.7 | 116.5 | **124.3** | 7.9 | 6.8% | **120.0** |
| Lansoprazole | 133.6 | 122.1 | 110.2 | **118.4** | 8.1 | 7.4% | **96.5** |
| Pantoprazole | - | 38.7 | 78.0 | **103.1** | 25.1 | 32.2% | **90.5** |
| Velcade | 50.8 | 58.1 | 72.9 | **95.1** | 22.2 | 30.5% | **100.0** |
| Colcrys | - | - | 33.6 | **51.9** | 18.4 | 54.8% | **60.0** |
| Dexilant | 18.1 | 24.2 | 32.7 | **50.3** | 17.6 | 53.6% | **56.0** |
| Nesina | 1.6 | 15.5 | 37.8 | **40.4** | 2.6 | 6.8% | **50.0** |
| Pioglitazone | 387.9 | 296.2 | 122.9 | **36.6** | -86.2 | -70.2% | **38.0** |
| Uloric | 9.1 | 12.9 | 17.7 | **26.9** | 9.2 | 51.6% | **31.0** |
| Actovegin | - | 9.8 | 19.6 | **26.4** | 6.8 | 34.7% | **25.5** |
| Amitiza | 18.6 | 18.7 | 22.3 | **25.7** | 3.3 | 15.0% | **27.5** |
| Calcium | - | 8.2 | 15.4 | **19.1** | 3.8 | 24.6% | **22.0** |
| Tachosil | - | 6.8 | 13.2 | **16.9** | 3.6 | 27.6% | **18.5** |
| Adcetris | - | 0.6 | 4.5 | **13.6** | 9.1 | - | **19.0** |

◆ **Ethical Drugs: Overseas major products' sales (Regional basis)**

(Billions of Yen)

| | FY10 | FY11 | FY12 | **FY13** | vs. FY12 | increase/ decrease | **FY14 Estimate** |
|---|---|---|---|---|---|---|---|
| Candesartan | | | | | | | |
| North America, Latin America, Europe, Russia/CIS, Asia and Others | 80.0 | 73.7 | 35.6 | **29.3** | -6.4 | -17.9% | **22.0** |
| Leuprorelin | | | | | | | |
| North America and Latin America | 14.7 | 16.1 | 14.9 | **16.4** | 1.4 | 9.7% | **14.0** |
| Europe and Russia/CIS | 31.0 | 30.5 | 27.8 | **33.3** | 5.5 | 19.7% | **36.0** |
| Asia and Other | 4.8 | 6.3 | 7.8 | **10.0** | 2.2 | 28.7% | **11.5** |
| Lansoprazole | | | | | | | |
| North America and Latin America | 42.8 | 24.3 | 24.5 | **29.7** | 5.2 | 21.2% | **16.0** |
| Europe and Russia/CIS | 16.4 | 16.8 | 10.5 | **12.8** | 2.3 | 21.5% | **11.5** |
| Asia and Other | 3.6 | 4.5 | 6.1 | **8.3** | 2.1 | 34.7% | **9.0** |
| Pantoprazole | | | | | | | |
| North America and Latin America | - | 12.8 | 28.9 | **39.8** | 11.0 | 37.9% | **20.5** |
| Europe and Russia/CIS | - | 17.9 | 29.9 | **36.3** | 6.4 | 21.2% | **42.0** |
| Asia and Other | - | 8.0 | 19.2 | **26.9** | 7.8 | 40.6% | **28.0** |
| Pioglitazone | | | | | | | |
| North America and Latin America | 306.2 | 244.5 | 90.9 | **6.2** | -84.7 | -93.2% | **12.0** |
| Europe and Russia/CIS | 29.5 | 15.8 | 8.2 | **7.8** | -0.4 | -4.8% | **7.0** |
| Asia and Other | 4.2 | 4.1 | 4.7 | **7.1** | 2.4 | 51.6% | **6.0** |

* This chart shows the major overseas products sales classified as "North America and Latin America", "Europe and Russia/CIS" and "Asia and Other" and does not include sales in Japan.

** The sales of Candesartan are shown in one area (North America, Latin America, Europe, Russia/CIS, Asia and Other) because export sales of Candesartan to licensees are recorded under a single route.

*** Effective from the FY12, the regional category of some countries in other than Americas was changed. For fair comparison, the amounts reported in the FY11 are modified according to the new classification.

## ◆ Ethical Drugs: Japan major products' sales

(Billions of Yen)

| Product | Launched | Therapeutic Class | FY10 | FY11 | FY12 | **FY13** | vs. FY12 | increase/ decrease | **FY14 Estimate **** |
|---|---|---|---|---|---|---|---|---|---|
| Blopress * (candesartan) | (99. 6) | Hypertension | 138.0 | 142.7 | 134.0 | **125.8** | -8.2 | -6.1% | **98.0** |
| Takepron * (lansoprazole) | (92.12) | Peptic ulcers | 70.9 | 76.5 | 69.1 | **67.6** | -1.4 | -2.1% | **60.0** |
| Leuplin (leuprorelin) | (92. 9) | Prostate cancer, breast cancer and endometriosis | 65.9 | 67.8 | 66.0 | **64.5** | -1.5 | -2.3% | **58.5** |
| Enbrel | (05. 3) | Rheumatoid arthritis | 38.4 | 41.4 | 43.2 | **45.4** | 2.2 | 5.1% | |
| Nesina * | (10. 6) | Diabetes | 1.6 | 15.5 | 37.8 | **38.0** | 0.2 | 0.6% | **36.5** |
| Azilva | (12. 5) | Hypertension | - | - | 3.4 | **25.3** | 21.9 | - | **46.5** |
| Vectibix | (10. 6) | Colorectal cancer | 9.4 | 17.2 | 18.8 | **19.4** | 0.5 | 2.8% | **18.5** |
| Basen | (94. 9) | Diabetes | 32.2 | 25.9 | 19.3 | **16.1** | -3.2 | -16.5% | **13.5** |
| Actos (pioglitazone) | (99.12) | Diabetes | 47.9 | 31.8 | 19.1 | **15.5** | -3.6 | -18.8% | **13.0** |
| Reminyl | (11. 3) | Alzheimer-type dementia | 0.5 | 2.7 | 8.4 | **12.3** | 3.9 | 46.1% | |
| Benet | (02. 5) | Osteoporosis | 17.6 | 16.5 | 13.3 | **11.6** | -1.7 | -13.0% | **9.5** |
| Rozerem | (10. 7) | Insomnia | 1.0 | 2.5 | 4.5 | **6.0** | 1.5 | 34.6% | **8.0** |
| Lotriga | (13. 1) | Hyperlipidemia | - | - | 1.1 | **5.2** | 4.2 | - | **12.0** |

* The figures include the amounts of compound drugs.

** The figures for "FY14 Estimate" are partially undisclosed due to disclosure policy of alliance partners.

## ◆ Consumer Healthcare: Major products' sales

(Billions of Yen)

| | FY10 | FY11 | FY12 | **FY13** | vs. FY12 | increase/ decrease | **FY14 Estimate** |
|---|---|---|---|---|---|---|---|
| Alinamin tablet | 14.0 | 14.7 | 15.7 | **19.6** | 4.0 | 25.2% | **17.9** |
| Alinamin drink | 12.7 | 13.0 | 14.3 | **15.1** | 0.7 | 5.2% | **14.7** |
| Benza | 8.7 | 9.2 | 9.7 | **10.4** | 0.7 | 7.2% | **10.7** |
| Biofermin | 7.0 | 7.5 | 8.1 | **8.4** | 0.3 | 3.9% | **8.4** |
| Borraginol | 4.2 | 4.3 | 4.3 | **4.4** | 0.0 | 1.1% | **4.2** |

## IV. Consolidated Statement of Cash Flows

(Billions of Yen)

| | FY10 (J-GAAP) | FY11 (J-GAAP) | FY12 (J-GAAP) | FY12 (IFRS) | **FY13 (IFRS)** | vs. FY12 |
|---|---|---|---|---|---|---|
| Net cash from operating activities | 326.9 | 336.6 | 307.7 | 332.6 | **148.3** | -184.2 |
| Income before income taxes and minority interests | 371.6 | 252.5 | 129.7 | | | |
| Net profit for the year | | | | 150.7 | **109.6** | -41.1 |
| Depreciation, amortization and impairment losses | 97.1 | 128.2 | 210.3 | 247.2 | **215.7** | -31.5 |
| Loss on voluntary recall of products | ― | ― | 4.3 | | | |
| Amortization of goodwill | 14.1 | 22.2 | 34.4 | | | |
| Loss (gain) on sales and disposal of property, plant and equipment | 0.9 | -16.8 | -1.5 | -2.6 | **-5.5** | -2.9 |
| Loss (gain) on sales of investment securities | -1.1 | -0.1 | -53.1 | -56.2 | **-40.5** | 15.8 |
| Equity in losses (earnings) of affiliates | -0.4 | 0.8 | -0.7 | | | |
| Interest on tax refund received | ― | ― | -15.1 | -15.1 | **―** | 15.1 |
| Income taxes | | | | -17.6 | **49.3** | 66.9 |
| Decrease (increase) in trade and other receivables * | -20.3 | 13.8 | 16.6 | 0.8 | **-42.5** | -43.3 |
| Decrease (increase) in inventories | -0.6 | 49.3 | -14.9 | -13.5 | **-16.9** | -3.5 |
| Increase (decrease) in trade and other payables * | 11.7 | 1.6 | 10.7 | -0.3 | **2.3** | 2.6 |
| Interest and dividends received | 6.1 | 6.3 | 5.1 | 5.3 | **4.6** | -0.7 |
| Interest paid | -1.3 | -1.9 | -3.2 | -3.2 | **-4.9** | -1.7 |
| Income tax paid | -141.8 | -152.1 | -22.7 | -22.7 | **-182.6** | -159.9 |
| Tax refund and interest on tax refund received | ― | ― | 57.2 | 57.2 | **15.3** | -42.0 |
| Other | -9.0 | 32.7 | -49.5 | 2.6 | **44.6** | 42.1 |
| Net cash from (used in) investing activities | -99.3 | -1,094.0 | -111.4 | -131.1 | **-158.6** | -27.5 |
| Net increase/decrease in time deposits | 15.9 | 0.4 | -1.5 | -1.5 | **-77.6** | -76.1 |
| Payments for acquisition of property, plant and equipment | -124.2 | -61.9 | -78.2 | -83.5 | **-50.1** | 33.3 |
| Proceeds from sales of property, plant and equipment | 0.7 | 21.1 | 8.1 | 8.1 | **13.4** | 5.3 |
| Payments for acquisition of intangible assets | -12.3 | -9.1 | -17.6 | -28.8 | **-28.4** | 0.4 |
| Net increase/decrease in marketable securities | 13.1 | 0.3 | -0.0 | | | |
| Net increase/decrease in investment securities | 3.8 | -0.4 | 58.3 | | | |
| Payments for acquisition of investment securities | | | | -2.0 | **-60.7** | -58.8 |
| Proceeds from sales and redemption of investment securities | | | | 63.8 | **48.9** | -14.9 |
| Payments for acquisition of subsidiaries' shares, resulting in consolidation scope change | ― | -1,040.0 | -86.3 | -86.3 | **-3.3** | 82.9 |
| Proceeds from sales of subsidiaries' shares, resulting in consolidation scope change | 3.4 | ― | 5.4 | 5.4 | **―** | -5.4 |
| Other | 0.4 | -4.3 | 0.3 | -6.4 | **-0.7** | 5.7 |
| Net cash from (used in) financing activities | -146.5 | 393.8 | -150.6 | -152.2 | **101.4** | 253.6 |
| Changes in short-term loans | -0.7 | 239.8 | -242.9 | -242.9 | **-0.6** | 242.3 |
| Proceeds from long-term loans | 1.3 | 110.0 | 0.3 | 0.3 | **130.0** | 129.7 |
| Payments of long-term loans | -1.3 | -0.1 | -0.2 | -0.2 | **-0.2** | 0.0 |
| Proceeds from issuance of bonds | ― | 189.6 | 238.0 | 238.0 | **119.7** | -118.3 |
| Dividends paid | -142.1 | -142.0 | -142.1 | -142.1 | **-142.1** | -0.0 |
| Other | -3.8 | -3.5 | -3.6 | -5.2 | **-5.3** | -0.1 |
| Effect of movements in exchange rates on cash and cash equivalents | -60.9 | -54.9 | 45.6 | | | |
| Net increase (decrease) in cash and cash equivalents | 20.2 | -418.5 | 91.3 | 49.3 | **91.2** | 41.9 |
| Cash and cash equivalents at beginning of year | 852.5 | 872.7 | 454.2 | 454.2 | **545.6** | 91.3 |
| Effect of movements in exchange rates on cash and cash equivalents | | | | 42.0 | **29.3** | -12.7 |
| Cash and cash equivalents at end of year | 872.7 | 454.2 | 545.6 | 545.6 | **666.0** | 120.5 |

* Item names under IFRS accounting. Figures in the J-GAAP colums apply to the J-GAAP definitions of:
・Decrease (increase) in trade and other receivables→Decrease (increase) in trade
・Increase (decrease) in trade and other payables→Increase (decrease) in trade

## V. Consolidated Statement of Financial Position（IFRS）

＜Assets＞ (Billions of Yen)

| | FY12 Beginning (IFRS) | FY12 End (IFRS) | **FY13 End (IFRS)** | % of Total | vs. FY12 End |
|---|---|---|---|---|---|
| Total non-current assets | 2,544.6 | 2,821.2 | **2,976.6** | 65.1% | 155.5 |
| Property, plant and equipment | 530.8 | 546.8 | **542.3** | 11.9% | -4.6 |
| acquisition cost | 1,072.6 | 1,109.0 | **1,167.7** | | 58.7 |
| Accumulated depreciation and impairment losses | -541.7 | -562.2 | **-625.4** | | -63.3 |
| Goodwill | 582.3 | 714.0 | **814.7** | 17.8% | 100.6 |
| Intangible assets | 1,026.8 | 1,095.8 | **1,135.6** | 24.9% | 39.8 |
| Investment property | 33.5 | 36.7 | **32.1** | 0.7% | -4.6 |
| Investments accounted for using the equity method | 8.3 | 9.2 | **10.0** | 0.2% | 0.8 |
| Other financial assets | 182.8 | 211.8 | **192.8** | 4.2% | -18.9 |
| Investment securities | 178.3 | 160.3 | **141.6** | | -18.7 |
| Other non-current assets | 17.8 | 27.5 | **40.8** | 0.9% | 13.2 |
| Prepaid pension costs | 12.8 | 23.3 | **35.8** | | 12.5 |
| Deferred tax assets | 162.3 | 179.4 | **208.4** | 4.6% | 29.1 |
| Total current assets | 1,061.7 | 1,231.4 | **1,592.5** | 34.9% | 361.1 |
| Inventories | 196.0 | 229.3 | **254.3** | 5.6% | 25.1 |
| Trade and other receivables | 357.1 | 375.0 | **430.6** | 9.4% | 55.6 |
| Other financial assets | 6.3 | 16.2 | **185.0** | 4.0% | 168.7 |
| Income tax receivables | 4.7 | 12.0 | **12.0** | 0.3% | 0.0 |
| Other current assets | 40.8 | 49.3 | **43.5** | 1.0% | -5.8 |
| Cash and cash equivalents | 454.2 | 545.6 | **666.0** | 14.6% | 120.5 |
| Assets held for sale | 2.4 | 4.0 | **1.0** | 0.0% | -3.0 |
| Total Assets | 3,606.2 | 4,052.6 | **4,569.1** | 100.0% | 516.6 |

**＜Liabilities and equity＞**

(Billions of Yen)

| | FY12 Beginning (IFRS) | FY12 End (IFRS) | **FY13 End (IFRS)** | % of Total | vs. FY12 End |
|---|---|---|---|---|---|
| Total liabilities | 1,438.4 | 1,714.3 | **2,028.5** | 44.4% | 314.2 |
| Total non-current liabilities | 679.2 | 1,080.4 | **1,225.8** | 26.8% | 145.3 |
| Bonds | 189.6 | 471.3 | **463.3** | 10.1% | -8.0 |
| Long-term loans | 111.4 | 111.3 | **241.3** | 5.3% | 129.9 |
| Other financial liabilities | 31.6 | 96.4 | **110.1** | 2.4% | 13.7 |
| Retirement benefit liabilities | 53.1 | 66.6 | **76.5** | 1.7% | 9.9 |
| Provisions | 16.1 | 21.8 | **14.4** | 0.3% | -7.4 |
| Other non-current liabilities | 14.9 | 41.1 | **39.6** | 0.9% | -1.6 |
| Deferred tax liabilities | 262.5 | 271.8 | **280.6** | 6.1% | 8.8 |
| Total current liabilities | 759.2 | 633.8 | **802.8** | 17.6% | 168.9 |
| Bonds | - | - | **154.1** | 3.4% | 154.1 |
| Short-term loans | 241.4 | 1.9 | **1.3** | 0.0% | -0.7 |
| Trade and other payables | 176.1 | 169.9 | **184.9** | 4.0% | 15.0 |
| Other financial liabilities | 11.5 | 38.6 | **48.8** | 1.1% | 10.3 |
| Income tax payables | 34.9 | 129.4 | **52.3** | 1.1% | -77.0 |
| Provisions | 110.4 | 100.8 | **125.3** | 2.7% | 24.5 |
| Other current liabilities | 184.9 | 193.3 | **236.0** | 5.2% | 42.6 |
| Total equity | 2,167.8 | 2,338.3 | **2,540.6** | 55.6% | 202.3 |
| Share capital | 63.5 | 63.5 | **63.6** | | 0.0 |
| Capital surplus | 50.1 | 40.3 | **39.9** | | -0.4 |
| Treasury shares | -0.8 | -0.6 | **-0.6** | | -0.0 |
| Retained earnings | 1,920.5 | 1,927.8 | **1,901.3** | | -26.5 |
| Other components of equity | 73.7 | 243.1 | **466.6** | | 223.5 |
| Equity attributable to owners of the company | 2,107.1 | 2,274.1 | **2,470.7** | | 196.6 |
| Non-controlling interests | 60.7 | 64.2 | **69.9** | | 5.7 |
| Total liabilities and equity | 3,606.2 | 4,052.6 | **4,569.1** | 100.0% | 516.6 |

## <Reference> Consolidated Balance Sheets (J-GAAP)

＜Assets＞ (Billions of Yen)

| | FY10 End (J-GAAP) | FY11 End (J-GAAP) | FY12 End (J-GAAP) | FY13 End (J-GAAP) | % of Total | vs. FY12 End |
|---|---|---|---|---|---|---|
| Current assets | 1,586.3 | 1,279.0 | 1,455.1 | 1,819.1 | 41.6% | 364.0 |
| Cash and time deposits | 217.9 | 214.9 | 289.6 | 432.9 | 9.9% | 143.3 |
| Securities | 656.3 | 240.7 | 258.1 | 372.8 | 8.5% | 114.7 |
| Notes and accounts receivable | 294.0 | 344.7 | 345.5 | 380.5 | 8.7% | 34.9 |
| Inventories | 137.1 | 195.0 | 229.5 | 254.2 | 5.8% | 24.7 |
| Deferred income taxes | 229.9 | 221.2 | 240.1 | 268.2 | 6.1% | 28.1 |
| Other current assets | 51.9 | 65.3 | 95.3 | 114.9 | 2.6% | 19.6 |
| Allowance for doubtful receivables | -0.9 | -2.9 | -3.2 | -4.4 | -0.1% | -1.3 |
| Fixed assets | 1,200.1 | 2,298.0 | 2,500.5 | 2,555.7 | 58.4% | 55.2 |
| Tangible fixed assets | 407.5 | 488.7 | 511.1 | 497.2 | 11.4% | -14.0 |
| Acquisition value | 856.4 | 1,015.0 | 1,073.5 | 1,123.8 | | 50.3 |
| Accumulated depreciation | -449.0 | -526.3 | -562.4 | -626.6 | | -64.2 |
| Intangible fixed assets | 517.4 | 1,516.2 | 1,689.7 | 1,796.3 | 41.1% | 106.5 |
| Goodwill | 217.1 | 582.3 | 675.4 | 725.6 | | 50.3 |
| Patents | 291.1 | 322.5 | 363.1 | 344.9 | | -18.1 |
| Sales rights | 2.0 | 570.2 | 582.9 | 628.3 | | 45.4 |
| Other intangible fixed assets | 7.2 | 41.3 | 68.5 | 97.4 | | 28.9 |
| Investment and other assets | 275.2 | 293.1 | 299.7 | 262.3 | 6.0% | -37.4 |
| Investment securities | 165.0 | 186.7 | 176.7 | 151.6 | | -25.1 |
| Long-term loans | 0.4 | 1.0 | 1.0 | 1.0 | | -0.0 |
| Prepaid pension costs | 32.6 | 27.0 | 28.8 | 43.8 | | 15.0 |
| Real estates for lease | 19.6 | 19.1 | 18.1 | 17.7 | | -0.4 |
| Deferred income taxes | 26.6 | 20.2 | 21.2 | 22.9 | | 1.7 |
| Others | 31.3 | 39.1 | 53.9 | 25.4 | | -28.5 |
| Allowance for doubtful receivables | -0.2 | -0.1 | -0.1 | -0.1 | | -0.1 |
| Total assets | 2,786.4 | 3,577.0 | 3,955.6 | 4,374.8 | 100.0% | 419.2 |

**＜Liabilities and net assets＞**

(Billions of Yen)

| | FY10 End (J-GAAP) | FY11 End (J-GAAP) | FY12 End (J-GAAP) | FY13 End (J-GAAP) | % of Total | vs. FY12 End |
|---|---|---|---|---|---|---|
| Total liabilities | 649.7 | 1,505.2 | 1,732.2 | 1,986.7 | 45.4% | 254.5 |
| Current liabilities | 436.6 | 751.7 | 613.6 | 763.7 | 17.5% | 150.0 |
| Notes and accounts payable | 83.1 | 101.9 | 118.7 | 129.8 | 3.0% | 11.1 |
| Short-term loans | 1.3 | 241.4 | 1.8 | 1.2 | 0.0% | -0.6 |
| Income taxes payable | 42.0 | 24.1 | 113.4 | 49.3 | 1.1% | -64.1 |
| Allowances and reserves | 53.0 | 47.2 | 83.3 | 88.9 | 2.0% | 5.7 |
| Other current liabilities | 257.2 | 337.1 | 296.4 | 494.3 | 11.3% | 197.9 |
| Long-term liabilities | 213.2 | 753.4 | 1,118.6 | 1,223.1 | 28.0% | 104.5 |
| Bond | - | 190.0 | 428.8 | 429.4 | 9.8% | 0.6 |
| Long-term loans | 1.3 | 111.4 | 111.3 | 241.3 | 5.5% | 129.9 |
| Reserve for retirement benefits | 16.8 | 54.4 | 60.2 | 71.5 | 1.6% | 11.3 |
| Reserve for directors' retirement | 1.1 | 1.3 | 1.5 | 1.5 | 0.0% | -0.0 |
| Deferred income taxes | 112.3 | 301.8 | 322.1 | 332.3 | 7.6% | 10.2 |
| Other long term liabilities | 81.7 | 94.6 | 194.7 | 147.1 | 3.4% | -47.6 |
| Net Assets | 2,136.7 | 2,071.9 | 2,223.4 | 2,388.1 | 54.6% | 164.7 |
| Shareholders' equity | 2,384.2 | 2,366.4 | 2,345.4 | 2,292.6 | | -52.9 |
| 〈Paid-in capital〉 | < 63.5> | < 63.5> | < 63.5> | < 63.6> | | < 0.0> |
| 〈Additional paid-in capital〉 | < 49.6> | < 49.6> | < 39.4> | < 38.3> | | < -1.0> |
| 〈Retained earnings〉 | < 2,272.1> | < 2,254.1> | < 2,243.1> | < 2,191.3> | | < -51.8> |
| 〈Treasury Stock〉 | < -1.0> | < -0.8> | < -0.6> | < -0.6> | | < -0.0> |
| Accumulated other comprehensive income | -292.6 | -354.6 | -186.4 | 25.1 | | 211.5 |
| 〈Unrealized gain on available-for-sales securities〉 | < 73.9> | < 87.0> | < 78.0> | < 66.5> | | < -11.5> |
| 〈Deferred hedge gains/losses〉 | < 0.0> | < 0.0> | < - > | < -0.5> | | < -0.5> |
| 〈Foreign currency translation adjustment〉 | < -366.6> | < -441.7> | < -264.4> | < -40.9> | | < 223.5> |
| Stock acquisition right | 0.3 | 0.5 | 0.9 | 1.5 | | 0.6 |
| Minority interests | 44.7 | 59.5 | 63.4 | 68.9 | | 5.5 |
| Total liabilities and net assets | 2,786.4 | 3,577.0 | 3,955.6 | 4,374.8 | 100.0% | 419.2 |

**VI. Segment Information**

(Billions of Yen)

| | FY10 (J-GAAP) | FY11 (J-GAAP) | FY12 (J-GAAP) | FY12 (IFRS) | **FY13 (IFRS)** | vs. FY12 | increase/ decrease |
|---|---|---|---|---|---|---|---|
| Net Sales | 1,419.4 | 1,508.9 | 1,557.3 | 1,557.0 | **1,691.7** | 134.7 | 8.6% |
| Ethical drugs | 1,267.4 | 1,358.8 | 1,401.7 | 1,401.5 | **1,529.1** | 127.5 | 9.1% |
| Japan | 578.5 | 592.2 | 588.4 | 588.2 | **582.1** | -6.1 | -1.0% |
| Overseas | 689.0 | 766.6 | 813.3 | 813.3 | **947.0** | 133.6 | 16.4% |
| Consumer healthcare | 60.3 | 61.7 | 66.9 | 66.9 | **72.9** | 6.0 | 8.9% |
| Others | 96.3 | 93.1 | 93.1 | 93.0 | **93.8** | 0.8 | 0.8% |
| Adjustments | -4.6 | -4.6 | -4.4 | -4.4 | **-4.0** | 0.4 | |
| Operating Income | 367.1 | 265.0 | 122.5 | 65.0 | **139.3** | 74.3 | 114.3% |
| Ethical drugs | 346.0 | 243.8 | 99.0 | 34.1 | **112.1** | 78.0 | - |
| <% of Ethical drugs sales/revenue> | <27.3%> | <17.9%> | <7.1%> | <2.4%> | **<7.3%>** | <4.9pt> | 0.0% |
| Consumer healthcare | 12.2 | 11.8 | 13.2 | 12.9 | **16.4** | 3.5 | 26.8% |
| <% of Consumer healthcare sales/revenue> | <20.3%> | <19.2%> | <19.7%> | <19.3%> | **<22.5%>** | <3.2pt> | 0.0% |
| Others | 11.0 | 11.7 | 12.4 | 17.9 | **10.8** | -7.1 | -39.8% |
| <% of Others sales/revenue> | <11.4%> | <12.6%> | <13.3%> | <19.3%> | **<11.5%>** | <-7.8pt> | 0.0% |
| Adjustments | -2.2 | -2.2 | -2.1 | 0.1 | **-0.0** | -0.1 | |

| | | | |
|---|---|---|---|
| Capital expenditures | 148.9 | 1,255.2 | 283.3 |
| Ethical drugs | 144.7 | * 1,249.1 | ** 275.6 |
| Consumer healthcare | 0.4 | 0.7 | 0.7 |
| Others | 3.7 | 5.4 | 7.0 |
| Adjustments | - | - | - |

* Including increase of intangible assets and goodwill due to acquisition of Nycomed.
** Including increase of intangible assets and goodwill due to acquisition of URL Pharma, Multilab, LigoCyte and Envoy.

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Depreciation and Amortization *** | 91.5 | 126.9 | 165.5 | 176.2 | **188.2** | 12.0 | 6.8% |
| Ethical drugs | 86.1 | 121.7 | 160.1 | 169.9 | **182.1** | 12.2 | 7.2% |
| Consumer healthcare | 0.8 | 0.8 | 0.8 | 0.8 | **0.7** | -0.1 | -9.8% |
| Others | 5.2 | 4.9 | 5.2 | 5.5 | **5.4** | -0.1 | -2.2% |
| Adjustments | -0.6 | -0.6 | -0.5 | - | **-** | - | |

*** Item name under IFRS accounting. Figures in the J-GAAP column apply to the J-GAAP definition of "Depreciation".

| | | | |
|---|---|---|---|
| Amortization of goodwill | 14.1 | 22.2 | 34.4 |
| Ethical drugs | 13.7 | 22.1 | 34.4 |
| Consumer healthcare | - | - | - |
| Others | 0.5 | 0.1 | 0.0 |
| Adjustments | - | - | - |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Impairment losses | | | | 71.0 | **27.5** | -43.4 | -61.2% |
| Ethical drugs | | | | 70.9 | **24.6** | -46.3 | -65.3% |
| Consumer healthcare | | | | - | **-** | - | - |
| Others | | | | 0.1 | **2.9** | 2.9 | - |
| Adjustments | | | | - | **-** | - | |

## VII. Number of employees

| | FY10 End | FY11 End | FY12 End | **FY13 End** | % of total | vs. FY12 End |
|---|---|---|---|---|---|---|
| Total (①－②)＋③ | 18,498 | 30,305 | 30,481 | **31,225** | 100.0% | 744 |
| < Overseas > | <9,031> | <20,775> | <20,956> | **<21,671>** | <69.4%> | <715> |
| Ethical drugs | 16,035 | 27,844 | 27,947 | **28,672** | 91.8% | 725 |
| Consumer healthcare | 435 | 440 | 450 | **461** | 1.5% | 11 |
| Others | 2,028 | 2,021 | 2,084 | **2,092** | 6.7% | 8 |
| Takeda Pharmaceutical Company Limited ① | 6,673 | 6,740 | 6,671 | **6,716** | | 45 |
| Temporarily transferred employees & Temporarily accepted employees (net) ② | 202 | 175 | 127 | **138** | | 11 |
| Employees working in Takeda Pharmaceutical Company Limited ①－② | 6,471 | 6,565 | 6,544 | **6,578** | 21.1% | 34 |
| Consolidated subsidiaries ③ | 12,027 | 23,740 | 23,937 | **24,647** | 78.9% | 710 |
| Affiliates (applied "equity method") | 772 | 762 | 639 | **656** | | 17 |

* Employees working in Takeda Pharmaceutical Company Limited on the full time equivalent basis

## VIII. Shareholders

### 【By ownership】

| | | FY10 End | FY11 End | FY12 End | **FY13 End** | vs. FY12 End |
|---|---|---|---|---|---|---|
| Financial Institutions | No. of shareholders | 335 | 333 | 311 | **313** | 2 |
| | No. of shares(1000) | 260,811 | 252,393 | 250,440 | **235,354** | -15,086 |
| | % of shares outstanding | 33.03 | 31.96 | 31.71 | **29.80** | -1.91 |
| Registered Financial Instruments Firms | No. of shareholders | 68 | 82 | 59 | **67** | 8 |
| | No. of shares(1000) | 39,030 | 41,967 | 37,273 | **38,582** | 1,309 |
| | % of shares outstanding | 4.94 | 5.32 | 4.72 | **4.88** | 0.16 |
| Other institutions | No. of shareholders | 1,726 | 1,937 | 1,772 | **1,890** | 118 |
| | No. of shares(1000) | 40,939 | 42,270 | 41,596 | **41,626** | 30 |
| | % of shares outstanding | 5.18 | 5.35 | 5.27 | **5.27** | 0.00 |
| Foreign investors | No. of shareholders | 929 | 849 | 861 | **883** | 22 |
| | No. of shares(1000) | 232,926 | 196,313 | 221,281 | **223,377** | 2,096 |
| | % of shares outstanding | 29.50 | 24.86 | 28.02 | **28.29** | 0.26 |
| Private investors and others | No. of shareholders | 253,232 | 301,426 | 275,841 | **305,206** | 29,365 |
| | No. of shares(1000) | 215,747 | 256,553 | 238,953 | **250,612** | 11,659 |
| | % of shares outstanding | 27.32 | 32.49 | 30.26 | **31.74** | 1.48 |
| Takeda | No. of shares(1000) | 213 | 170 | 123 | **130** | 7 |
| | % of shares outstanding | 0.03 | 0.02 | 0.02 | **0.02** | 0.00 |

### 【By number of shares held each】

| | | FY10 End | FY11 End | FY12 End | **FY13 End** | vs. FY12 End |
|---|---|---|---|---|---|---|
| 5,000,000～ | No. of shareholders | 24 | 24 | 25 | **21** | -4 |
| | No. of shares(1000) | 297,487 | 289,885 | 300,172 | **267,568** | -32,604 |
| | % of shares outstanding | 37.67 | 36.71 | 38.01 | **33.88** | -4.13 |
| 1,000,000～ 4,999,999 | No. of shareholders | 84 | 74 | 79 | **91** | 12 |
| | No. of shares(1000) | 198,059 | 175,690 | 176,679 | **203,000** | 26,320 |
| | % of shares outstanding | 25.08 | 22.25 | 22.37 | **25.71** | 3.33 |
| 100,000～ 999,999 | No. of shareholders | 297 | 275 | 288 | **273** | -15 |
| | No. of shares(1000) | 96,821 | 85,621 | 92,399 | **85,950** | -6,449 |
| | % of shares outstanding | 12.26 | 10.84 | 11.70 | **10.88** | -0.82 |
| 10,000～ 99,999 | No. of shareholders | 2,146 | 2,516 | 2,373 | **2,472** | 99 |
| | No. of shares(1000) | 46,007 | 52,587 | 49,309 | **50,889** | 1,580 |
| | % of shares outstanding | 5.83 | 6.66 | 6.25 | **6.46** | 0.21 |
| 1,000～ 9,999 | No. of shareholders | 53,397 | 65,273 | 60,392 | **63,080** | 2,688 |
| | No. of shares(1000) | 105,897 | 129,691 | 120,618 | **126,265** | 5,647 |
| | % of shares outstanding | 13.41 | 16.42 | 15.28 | **16.00** | 0.71 |
| 100～ 999 | No. of shareholders | 190,886 | 226,498 | 206,147 | **232,953** | 26,806 |
| | No. of shares(1000) | 45,134 | 55,921 | 50,234 | **55,762** | 5,528 |
| | % of shares outstanding | 5.72 | 7.08 | 6.36 | **7.06** | 0.70 |
| Less than 99 | No. of shareholders | 9,457 | 9,968 | 9,541 | **9,470** | -71 |
| | No. of shares(1000) | 261 | 271 | 255 | **247** | -8 |
| | % of shares outstanding | 0.03 | 0.04 | 0.03 | **0.03** | -0.00 |
| Total | No. of shareholders | 256,291 | 304,628 | 278,845 | **308,360** | 29,515 |
| | No. of shares(1000) | 789,666 | 789,666 | 789,666 | **789,681** | 14 |

### 【10 largest shareholders】

| | Shareholders | **March 31, 2014** | | Change from March 31, 2013 | |
|---|---|---|---|---|---|
| | | **No. of shares held (1000)** | **% of shares outstanding** | No. of shares increase/ decrease | Previous ranking |
| **1** | Nippon Life Insurance Company | **53,580** | **6.79** | -2,820 | <1> |
| **2** | The Master Trust Bank of Japan, Ltd. (Trust account) | **32,728** | **4.14** | -1,124 | <3> |
| **3** | Japan Trustee Services Bank, Ltd. (Trust account) | **29,887** | **3.78** | -4,849 | <2> |
| **4** | Takeda Science Foundation | **17,912** | **2.27** | - | <4> |
| **5** | Barclays Securities Japan Limited | **15,000** | **1.90** | 3,000 | <6> |
| **6** | The Bank of New York 133522 | **10,680** | **1.35** | 10,680 | - |
| **7** | State Street Trust & Banking Co., Ltd. 505225 | **9,582** | **1.21** | -886 | <7> |
| **8** | State Street Bank West Client-Treaty | **9,315** | **1.18** | 2,282 | <12> |
| **9** | Japan Trustee Services Bank, Ltd. (Trust account 6) | **8,179** | **1.04** | 1,232 | <14> |
| **10** | Japan Trustee Services Bank, Ltd. (Trust account 5) | **8,169** | **1.03** | 2,741 | <24> |

## X. Financial ratios

| | FY10 (J-GAAP) | FY11 (J-GAAP) | FY12 (J-GAAP) | FY13 (J-GAAP) | FY12 (IFRS) | **FY13 (IFRS)** |
|---|---|---|---|---|---|---|
| ［Growth rates］ | | | | | | |
| Net sales (%) | -3.2 | 6.3 | 3.2 | 8.6 | | **8.6** |
| Operating income (%) | -12.6 | -27.8 | -53.8 | 27.1 | | **114.3** |
| Net income (%) | -16.8 | -49.9 | 5.7 | -31.2 | | **-28.2** |
| ［Profitability ratios］ | | | | | | |
| Gross Profit margin (%) | 77.6 | 71.3 | 70.4 | 71.1 | 70.2 | **71.0** |
| Operating margin (%) | 25.9 | 17.6 | 7.9 | 9.2 | 4.2 | **8.2** |
| Net margin (%) | 17.5 | 8.2 | 8.4 | 5.3 | 9.5 | **6.3** |
| Return on assets (%) | 8.8 | 3.9 | 3.5 | 2.2 | 3.9 | **2.5** |
| ROE（Return on equity）(%) | 11.8 | 6.1 | 6.3 | 4.0 | 6.8 | **4.5** |
| ［Stability ratios］ | | | | | | |
| Equity to assets (%) | 75.1 | 56.2 | 54.6 | 53.0 | 56.1 | **54.1** |
| Current ratio (%) | 363.3 | 170.1 | 237.1 | 238.2 | 194.3 | **198.4** |
| Fixed assets to long-term capital (%) | 52.1 | 83.1 | 76.3 | 72.2 | 84.1 | **80.5** |
| ［Efficiency ratios］ | | | | | | |
| Asset turnover (times) | 0.51 | 0.42 | 0.39 | 0.39 | 0.38 | **0.37** |
| Fixed-asset turnover (times) | 1.18 | 0.66 | 0.62 | 0.66 | 0.55 | **0.57** |
| Notes and accounts receivable turnover (times) | 4.83 | 4.38 | 4.51 | 4.45 | 4.50 | **4.45** |
| ［Other ratios］ | | | | | | |
| R&D expenses to net sales (%) | 20.4 | 18.7 | 20.8 | 20.3 | 20.6 | **20.2** |
| BPS (Book value of equity per share) (Yen) | 2,650 | 2,549 | 2,735 | 2,936 | 2,881 | **3,130** |
| EPS (Earnings per share) (Yen) | 314.01 | 157.29 | 166.25 | 114.44 | 188.21 | **135.10** |
| Growth Rate of EPS (%) | -16.8 | -49.9 | 5.7 | -31.2 | | **-28.2** |
| Payout ratio (%) | 57.3 | 114.4 | 108.3 | 157.3 | 95.6 | **133.2** |
| DOE（Dividend on equity）(%) | 6.7 | 6.9 | 6.8 | 6.3 | 6.5 | **6.0** |

* Ratios under IFRS are calculated from "Revenue", "Profit attributable to owners of the company" and "Equity attributable to owners of the Company", instead of "Net sales", "Net income" and "Shareholders' equity" under J-GAAP, respectively.
** "Notes and accounts receivable turnover" are after adjustment of outstanding balance at each fiscal year end and/or 1st half of fiscal year if the ending day falls on weekend or holiday, and to be paid on the beginning day of the following fiscal term.

# Ⅹ. Pipeline

**Development Activities**

- ■ Compounds
- ■ Additional indications/formulations of compounds
- ■ Recent progress in stage
- ■ Discontinued project
- ■ Revised collaboration agreement
- ■ Selected Filings and Approvals in Regions other than US/EU/Jpn
- ■ Characteristics of projects
- ■ Other alliance projects
- ■ Clinical study protocol summaries
- ■ Outcome studies

**Research Activities**

- ■ Main joint research activities

## (5) Development activities

Note: This table primarily shows the indications for which we will actively pursue approval. We are also conducting additional studies of certain assets to examine their potential for use in further indications.

### ■ US/EU/Jpn

| Development code/product name <generic name> | Drug Class (administration route) | Indications | Stage | | In-house/ In-license |
|---|---|---|---|---|---|
| **TAK-390MR <dexlansoprazole>** | Proton pump inhibitor (oral) | Erosive esophagitis (healing and maintenance), Non-erosive gastro-esophageal reflux disease | EU | Approved (Sep 13)*1 | In-house |
| **SYR-322 <alogliptin>** | DPP-4 inhibitor (oral) | Diabetes mellitus | EU | Approved (Sep 13) | In-house |
| | | Diabetes mellitus (Fixed-dose combination with metformin) | EU | Approved (Sep 13) | |
| | | Diabetes mellitus (Fixed-dose combination with pioglitazone) | EU | Approved (Sep 13) | |
| **ATL-962 <cetilistat>** | Lipase inhibitor (oral) | Obesity with both type 2 diabetes mellitus and dyslipidemia | Jpn | Approved (Sep 13) | In-license (Norgine BV)*2 |
| **Lu AA21004 <vortioxetine>** | Multimodal anti-depressant (oral) | Major depressive disorder | US<br>Jpn | Approved (Sep 13)<br>P-III | In-license (Lundbeck) |
| | | Generalized anxiety disorder | US | P-III | |
| **SGN-35 <brentuximab vedotin>** | CD30 monoclonal antibody-drug conjugate (injection) | Relapsed or refractory Hodgkin lymphoma | Jpn | Approved (Jan 14) | In-license (Seattle Genetics) |
| | | Relapsed or refractory anaplastic large cell lymphoma | Jpn | Approved (Jan 14) | |
| | | Relapsed cutaneous T-cell lymphoma | EU | P-III | |
| | | Post-ASCT Hodgkin lymphoma | EU | P-III | |
| | | Front line Hodgkin lymphoma | EU<br>JP | P-III<br>P-III | |
| | | Front line mature T-cell lymphoma | EU<br>Jpn | P-III<br>P-III | |
| **BLB-750** | Influenza vaccine (injection) | Prevention of pandemic influenza | Jpn | Approved (Mar 14) | In-license (Baxter) |
| **<lurasidone hydrochloride>** | Atypical antipsychotic agent (oral) | Schizophrenia | EU | Approved (Mar 14) | In-license (Dainippon Sumitomo) |
| | | Bipolar disorder | EU | P-III | |
| **MLN0002 <vedolizumab>** | Humanized monoclonal antibody against α4β7 integrin (injection) | Ulcerative colitis | US<br>EU<br>Jpn | Filed (Jun 13)<br>Filed (Mar 13)<br>P-III | In-house |
| | | Crohn's disease | US<br>EU<br>Jpn | Filed (Jun 13)<br>Filed (Mar 13)<br>P-III | |
| **TAK-438 <vonoprazan>** | Potassium-competitive acid blocker (oral) | Acid-related diseases (GERD, Peptic ulcer, etc.) | Jpn | Filed (Feb 14) | In-house |
| **SYR-472 <trelagliptin>** | DPP-4 inhibitor (oral) | Diabetes mellitus | Jpn<br>US<br>EU | Filed (Mar 14)<br>P-II<br>P-II | In-house |
| **TAK-816** | Hib vaccine (injection) | Prevention of infectious disease caused by *Haemophilus influenzae* type b (Hib) | Jpn | Filed (Sep 13) | In-license (Novartis) |
| **Contrave® <naltrexone SR /bupropion SR>** | Mu-opioid receptor antagonist and dopamine/norepinephrine re-uptake inhibitor (oral) | Obesity | US | Filed (Dec 13) | In-license (Orexigen) |
| **<fomepizole>** | Alcohol dehydrogenase inhibitor (injection) | Ethylene glycol and methanol poisonings | Jpn | Filed (Dec 13) | In-license (Paladin Labs) |

*1 Approved in 16 countries in the EU by the decentralized procedure

*2 Alizyme assigned ATL-962 (cetilistat) business to Norgine BV on Oct 15th, 2009

| Development code/product name <generic name> | Drug Class (administration route) | Indications | Stage | | In-house/ In-license |
|---|---|---|---|---|---|
| **TAK-700 <orteronel>** | Non-steroidal androgen synthesis inhibitor (oral) | Prostate cancer | US<br>EU<br>Jpn | P-III<br>P-III<br>P-III | In-house |
| **MLN9708 <ixazomib>** | Proteasome inhibitor (oral) | Previously untreated multiple myeloma | US<br>EU<br>Jpn | P-III<br>P-III<br>P-III | In-house |
| | | Relapsed or refractory multiple myeloma | US<br>EU<br>Jpn | P-III<br>P-III<br>P-III | |
| | | Relapsed or refractory primary (AL) amyloidosis | US<br>EU | P-III<br>P-III | |
| | | Solid tumors | US | P-I | |
| **MLN8237 <alisertib>** | Aurora A kinase inhibitor (oral) | Relapsed or refractory peripheral T-cell lymphoma | US<br>EU | P-III<br>P-III | In-house |
| | | Small cell lung cancer, Ovarian cancer | US<br>EU | P-II<br>P-II | |
| | | Non-Hodgkin lymphoma | Jpn | P-I | |
| | | Solid tumors | Jpn | P-I | |
| **<motesanib diphosphate>** | VEGFR1-3, PDGFR, c-Kit inhibitor (oral) | Advanced non-squamous non-small cell lung cancer | Jpn | P-III | In-license (Amgen) |
| **AMG 386 <trebananib>** | Anti-angiopoietin peptibody (injection) | Ovarian cancer | Jpn | P-III | In-license (Amgen) |
| **<peginesatide>** | Synthetic, peptide-based erythropoiesis-stimulating agent (injection) | Anaemia associated with chronic kidney disease in adult patients undergoing dialysis | EU | P-III*3 | In-license (Affymax) |
| **TAK-385 <relugolix>** | LH-RH antagonist (oral) | Endometriosis | Jpn | P-II | In-house |
| | | Uterine fibroids | Jpn | P-II | |
| | | Prostate Cancer | US | P-II | |
| **MLN0128 < - >** | mTORC1/2 inhibitor (oral) | Breast cancer | US | P-II | In-house |
| | | Solid tumors | - | P-I | |
| **TAK-003***4 | Tetravalent Dengue vaccine (injection) | Prevention of dengue fever caused by dengue virus | - | P-II | In-house |
| **Norovirus vaccine** | Norovirus vaccine (injection) | Prevention of acute gastroenteritis (AGE) caused by norovirus | - | P-II | In-house |
| **TAK-114***5 | Pro-inflammatory cytokine inhibitor (oral) | Ulcerative colitis | - | P-II | In-license (Natrogen) |
| **TAK-361S** | Tetravalent vaccine (injection) | Prevention of infectious disease caused by Diphtheria, Pertussis, Tetanus, Poliomyelitis | Jpn | P-II | In-license (Japan Polio research institute) |
| **MT203 <namilumab>** | GM-CSF monoclonal antibody (injection) | Psoriasis | EU | P-II | In-licence (Amgen)*6 |
| | | Rheumatoid arthritis | EU | P-I | |
| **TAK-850** | Influenza vaccine (injection) | Prevention of influenza disease caused by influenza virus subtype A and B contained in the vaccine | Jpn | P-I/II | In-license (Baxter) |
| **TAK-733 < - >** | MEK inhibitor (oral) | Solid tumors | - | P-I | In-house |
| **TAK-272 < - >** | Direct renin inhibitor (oral) | Hypertension | - | P-I | In-house |
| **TAK-063 < - >** | PDE10A inhibitor (oral) | Schizophrenia | - | P-I | In-house |

*3 Resubmission subject to outcome of ongoing investigation in the US

*4 Formerly known as DENVax

*5 Formerly known as Natura-alpha

*6 Deal made with Micromet; on Mar 7th, 2012, Micromet became a wholly owned subsidiary of Amgen

| Development code/ product name <generic name> | Drug Class (administration route) | Indications | Stage | | In-house/ In-license |
|---|---|---|---|---|---|
| **TAK-137 < - >** | AMPA receptor potentiator (oral) | Psychiatric disorders and neurological diseases | - | P-I | In-house |
| **TAK-659 < - >** | SYK kinase inhibitor (oral) | Solid tumors, Hematologic malignancies | - | P-I | In-house |
| **TAK-233 < - >** | (oral) | - | - | P-I | In-house |
| **INV21** | EV71 vaccine (injection) | Prevention of hand, foot and mouth disease caused by enterovirus 71 | - | P-I | In-house |
| **MLN4924 < - >** | NEDD 8 activating enzyme inhibitor (injection) | Advanced malignancies | - | P-I | In-house |
| **MLN1117 < - >** | PI3Kα isoform inhibitor (oral) | Solid tumors | - | P-I | In-house |
| **MLN0264 < - >** | Antibody-Drug Conjugate targeting GCC (injection) | Advanced gastrointestinal malignancies | - | P-I | In-house |
| **MLN7243 < - >** | UAE Inhibitor (injection) | Solid tumors | - | P-I | In-house |
| **MLN2480 < - >** | pan-Raf kinase inhibitor (oral) | Solid tumors | - | P-I | In-license (Sunesis) |
| **ITI-214 < - >** | PDE1 inhibitor (oral) | Cognitive impairment associated with schizophrenia | - | P-I | In-license (Intra-Cellular) |
| **Lu AA24530 < - >** | Multimodal anti-depressant (oral) | Major depressive disorder, Generalized anxiety disorders | US<br>Jpn | P-I<br>P-I | In-license (Lundbeck) |
| **AMG 403 <fulranumab>** | Human monoclonal antibody against human Nerve Growth Factor (NGF) (injection) | Pain | Jpn | P-I | In-license (Amgen) |
| **<rasagiline>** | Monoamine oxidase B (MAO-B) inhibitor (oral) | Parkinson's disease | Jpn | P-I | In-license (Teva) |

## ■ Additional indications/formulations of compounds

| Development code/ product name <generic name> Brand name (country / region) | Drug Class | Indications or formulations | Stage | In-house/ In-license |
|---|---|---|---|---|
| **AG-1749 <lansoprazole>** Takepron® (Jpn) Prevacid® (US) Ogast®, etc. (EU) | Proton pump inhibitor | Fixed-dose combination with low-dose aspirin | Jpn Approved (Mar 14) | In-house |
| **TAK-536 <azilsartan>** Azilva® (Jpn) | Angiotensin II receptor blocker | Hypertension (Fixed-dose combination with amlodipine besilate) | Jpn Approved (Mar 14) | In-house |
| **RIENSO® <ferumoxytol>** | IV iron | Iron deficiency anemia from all causes in patients who have a history of unsatisfactory oral iron therapy or in whom oral iron cannot be used | EU Filed (Jun 13) | In-license (AMAG) |
| **TAP-144-SR <leuprorelin acetate>** Leuplin® (Jpn) Lupron Depot® (US) Enantone®, etc. (EU) | LH-RH agonist | Prostate cancer, Premenopausal breast cancer (6-month formulation) | Jpn P-III | In-house |
| **TAK-375SL <ramelteon>** Rozerem® (US, Jpn) | MT1/MT2 receptor agonist | Bipolar (sublingual formulation) | US P-III | In-house |
| **VELCADE® <bortezomib>** | Proteasome inhibitor | Front line mantle cell lymphoma<br>Relapsed diffuse large B-cell lymphoma | US P-III<br>US P-III | In-house |
| **AD-4833/TOMM40** | Insulin sensitizer/ Biomarker assay | Delay of onset of mild cognitive impairment due to Alzheimer's disease | US P- III<br>EU P- III | In-license (Zinfandel) |
| **AMITIZA® <lubiprostone>** | Chloride channel activator | Liquid formulation<br>Pediatric functional constipation | US P- III<br>US P- III | In-license (Sucampo) |

| | | | | |
|---|---|---|---|---|
| **TMX-67XR <febuxostat>** Uloric® (US) | Non-purine, selective xanthine oxidase inhibitor | Extended-release formulation | US P- III | In-license (Teijin) |
| **TAK-390MROD <dexlansoprazole>** Dexilant® (US) | Proton pump inhibitor | Orally disintegrating tablet | - P-I | In-house |

## ■ Recent progress in stage **Progress in stage since release of FY2012 results (May 9th, 2013)**

| Development code/ product name <generic name> | Indications | Country/Region | Progress in stage |
|---|---|---|---|
| **TAK-390MR <dexlansoprazole>** | Erosive esophagitis (healing and maintenance), Non-erosive gastro-esophageal reflux disease | EU | Approved (Sep 13) |
| **SYR-322 <alogliptin>** | Diabetes mellitus | EU | Approved (Sep 13) |
| **SYR-322 <alogliptin>** | Diabetes mellitus (Fixed-dose combination with metformin) | EU | Approved (Sep 13) |
| **SYR-322 <alogliptin>** | Diabetes mellitus (Fixed-dose combination with pioglitazone) | EU | Approved (Sep 13) |
| **ATL-962 <cetilistat>** | Obesity with both type 2 diabetes mellitus and dyslipidemia | Jpn | Approved (Sep 13) |
| **Lu AA21004 <vortioxetine>** | Major depressive disorder | US | Approved (Sep 13) |
| **SGN-35 <brentuximab vedotin>** | Relapsed or refractory Hodgkin lymphoma | Jpn | Approved (Jan 14) |
| **SGN-35 <brentuximab vedotin>** | Relapsed or refractory anaplastic large cell lymphoma | Jpn | Approved (Jan 14) |
| **MLN0002 <vedolizumab>** | Ulcerative colitis | US | Filed (Jun 13) |
| **MLN0002 <vedolizumab>** | Crohn's disease | US | Filed (Jun 13) |
| **RIENSO® <ferumoxytol>** | Iron deficiency anemia from all causes in patients who have a history of unsatisfactory oral iron therapy or in whom oral iron cannot be used | EU | Filed (Jun 13) |
| **TAK-816** | Prevention of infectious disease caused by *Haemophilus influenzae* type b (Hib) | Jpn | Filed (Sep 13) |
| **Contrave® <naltrexone SR / bupropion SR>** | Obesity | US | Filed (Dec 13) |
| **<fomepizole>** | Ethylene glycol and methanol poisonings | Jpn | Filed (Dec 13) |
| **AD-4833/TOMM40** | Delay of onset of mild cognitive impairment due to Alzheimer's disease | US/EU | P-III |
| **AMITIZA® <lubiprostone>** | Liquid formulation | US | P-III |
| **AMITIZA® <lubiprostone>** | Pediatric functional constipation | US | P-III |
| **SGN-35 <brentuximab vedotin>** | Front line mature T-cell lymphoma | Jpn | P-III |
| **MLN0002 <vedolizumab>** | Ulcerative colitis | Jpn | P-III |
| **MLN0002 <vedolizumab>** | Crohn's disease | Jpn | P-III |
| **MLN9708 <ixazomib>** | Relapsed or refractory multiple myeloma | Jpn | P-III |
| **TAK-137 < - >** | Psychiatric disorders and neurological diseases | - | P-I |
| **TAK-659 < - >** | Hematologic malignancies, Solid tumors | - | P-I |
| **AG-1749 <lansoprazole>** | Fixed-dose combination with low-dose aspirin | Jpn | Approved (Mar 14) |
| **TAK-536 <azilsartan>** | Hypertension (Fixed-dose combination with amlodipine besilate) | Jpn | Approved (Mar 14) |
| **BLB-750** | Prevention of pandemic influenza | Jpn | Approved (Mar 14) |
| **<lurasidone hydrochloride>** | Schizophrenia | EU | Approved (Mar 14) |
| **TAK-438 <vonoprazan>** | Acid-related diseases (GERD, Peptic ulcer, etc.) | Jpn | Filed (Feb 14) |

| | | | |
|---|---|---|---|
| **SYR-472 <trelagliptin>** | Diabetes mellitus | Jpn | Filed (Mar 14) |
| **TMX-67XR <febuxostat>** | Extended-release formulation | US | P-III |
| **SGN-35 <brentuximab vedotin>** | Front line Hodgkin lymphoma | Jpn | P-III |
| **TAK-385 <relugolix>** | Prostate cancer | US | P-II |
| **MLN0128 < - >** | Breast cancer | US | P-II |
| **MT203 <namilumab>** | Psoriasis | EU | P-II |
| **Norovirus vaccine** | Prevention of acute gastroenteritis (AGE) caused by norovirus | - | P-II |
| **TAK-850** | Prevention of influenza disease caused by influenza virus subtype A and B contained in the vaccine | Jpn | P-I/II |
| **TAK-233 < - >** | - | - | P-I |
| **TAK-390MR OD <dexlansoprazole>** | Delayed-release orally disintegrating tablet | - | P-I |
| **MLN7243 < - >** | Solid tumors | - | P-I |

Progress in stage since the announcement of FY2013 3Q results (February 5th, 2014) are listed under the bold dividing line

## ■ Discontinued projects **Discontinued since release of FY2012 results (May 9th, 2013)**

| Development code/ product name <generic name> | Indications (Stage) | Reason |
|---|---|---|
| **AMG 479 <ganitumab>** | Metastatic pancreas cancer (Jpn P-III) | Independent Data Monitoring Committee (DMC) reviewed the interim analysis and concluded that it was unlikely to meet the primary endpoint |
| **TAK-491 <azilsartan medoxomil>** | Hypertension (fixed-dose combination with chlorthalidone) (EU P-III) | Discontinued due to a reassessment of the marketing opportunity in the EU |
| **TAK-428 < - >** | Diabetic neuropathy (US/EU P-II) | Discontinued based on reassessment of portfolio prioritization |
| **TAK-390MR <dexlansoprazole>** | Erosive esophagitis (healing and maintenance), Non-erosive gastro-esophageal reflux disease (Jpn P-II) | Discontinued due to advanced progress of TAK-438 program in Japan |
| **TAK-329 < - >** | Diabetes (P-I) | Discontinued due to the clinical data failing to meet the criteria for stage-up |
| **TAK-875 <fasiglifam>** | Diabetes (P-III) | Discontinued due to concerns about liver safety |

## ■ Revised collaboration agreement **Revised since release of FY2012 results (May 9th, 2013)**

| Development code/ product name <generic name> | Indications (Stage) | Reason |
|---|---|---|
| **Sovrima® <idebenone>** | Friedreich's ataxia, Duchenne muscular dystrophy (EU P-III) | Rights for Sovrima returned to Santhera upon Santhera's request and due to a reassessment of portfolio prioritization |
| **<veltuzumab>** | Systemic lupus erythematosus (US/EU P-II) | The agreement on veltuzumab with Immunomedics terminated; an arbitration proceeding between the parties is currently on-going |

## ■ Selected Filings and Approvals in Regions other than US/EU/Jpn (not comprehensive)

| Region | Country | Development code / product name (stage) |
|---|---|---|
| Americas Ex. US | Argentina | TAK-491*7 (Approved Nov 13), SGN-35 (Filed Jun 13), SYR-322 (Filed Aug 13), SYR-322/metformin (Filed Sep 13), SYR-322/pioglitazone (Filed Sep 13) |
| | Brazil | SYR-322 (Approved Dec 13), TAK-491 (Filed Nov 11), SYR-322/metformin (Filed Jun 12), TAK-491/chlorthalidone (Filed Jun 12), SYR-322/pioglitazone (Filed Dec 12) , SGN-35 (Filed Feb 13), TAK-375*8 (Filed Mar 14) |
| | Colombia | roflumilast*9 (Approved Jul 13), TAK-390MR (Approved Feb 14), TAK-491 (Filed Aug 12), SYR-322 (Filed Sep 12), TAK-491/chlorthalidone (Filed Oct 12),SYR-322/pioglitazone (Filed Oct 12), SYR-322/metformin (Filed Nov 12), SGN-35 (Filed Feb 13) |
| | Ecuador | roflumilast (Approved Nov 13), TAK-491 (Approved Feb 14), TAK-390MR (Approved Feb 14), TAK-491/chlorthalidone (Approved Mar 14), SYR-322 (Filed Nov 13), SYR-322/pioglitazone (Filed Nov 13), SYR-322/metformin (Filed Nov 13) |
| | Mexico | SGN-35 (Orphan Drug Approval Nov 13) |
| | Peru | TAK-390MR (Filed Aug 13), SYR-322 (Filed Dec 13), SYR-322/pioglitazone (Filed Dec 13), TAK-491/chlorthalidone (Filed Mar 14), SGN-35 (Filed Mar 14) |
| | Venezuela | mifamurtide*10 (Approved Apr 13), roflumilast (Approved Jul 13), SGN-35 (Medical Service Product Approved Jan 14, Full NDA filed Nov 13), TAK-390MR (Filed Sep 13), TAK-491/chlorthalidone (Filed Nov 13), SYR-322 (Filed Apr 14), SYR-322/metformin (Filed Apr 14) |
| Europe Ex. EU | Iceland | SYR-322 (Approved Oct 13), SYR-322/metformin (Approved Oct 13), SYR-322/pioglitazone (Approved Oct 13) |
| | Norway | SYR-322 (Approved Oct 13), SYR-322/metformin (Approved Oct 13), SYR-322/pioglitazone (Approved Oct 13) |
| | Switzerland | lurasidone hydrochloride (Approved Aug 13), SYR-322 (Approved Nov 13), SYR-322/metformin (Approved Nov 13), TAK-390MR (Filed Sep 12), TAK-491/chlorthalidone (Filed Jan 13), MLN0002 (Filed May 13) |
| Russia/CIS | Kazakhstan | TAK-491 (Approved Oct 13), SGN-35 (Filed Sep 12), TAK-390MR (Filed Oct 13), SYR-322 (Filed Feb 14) |
| | Russia | TAK-491 (Approved Feb 14), TAK-390MR (Filed Jul 13), SYR-322 (Filed Dec 13), SYR-322/metformin (Filed Dec 13) |
| | Ukraine | mifamurtide (Approved Jul 13), SGN-35 (Approved Oct 13), TAK-491 (Approved Nov 13), TAK-390MR (Filed Jul 13), SYR-322 (Filed Jan 14), SYR-322/metformin (Filed Feb 14) |
| Asia Ex. Jpn | China | SYR-322 (Approved Jul 13), roflumilast (Filed Dec 11), SGN-35 (Filed May 13) |
| | Hong Kong | SGN-35 (Filed Feb 13), TAK-491/chlorthalidone (Filed Mar 13), TAK-491 (Filed Oct 13), SYR-322 (Filed Dec 13), SYR-322/metformin (Filed Dec 13), |
| | India | roflumilast (Filed Mar 13) |
| | Indonesia | SYR-322 (Filed Jan 11), TAK-491 (Filed Feb 12), TAK-491/chlorthalidone (Filed Jul 12), TCV-116*11/amlodipine besilate (Filed Oct 12) |
| | Malaysia | TAK-390MR (Approved Jan 14), TAK-491 (Filed Jan 13), TAK-491/chlorthalidone (Filed Apr 13), SYR-322 (Filed Dec 13), SYR-322/metformin (Filed Dec 13), SYR-322/pioglitazone (Filed Dec 13) |
| | Philippines | TAK-491/chlorthalidone (Filed Sep 13) |
| | Singapore | SGN-35 (Approved Jan 14), TAK-390MR (Approved Jan 14), TAK-491 (Filed Dec 12), TAK-491/chlorthalidone (Filed Mar 13), SYR-322 (Filed Jan 14), SYR-322/metformin (Filed Mar 14) |
| | S. Korea | SYR-322 (Approved May 13), SGN-35 (Approved May 13), SYR-322/pioglitazone (Filed Nov 13) |
| | Taiwan | TAK-491 (Approved Jun 13), SYR-322 (Filed Mar 11), TAK-491/chlorthalidone (Filed May 12), TCV-116/amlodipine besilate (Filed Nov 12), SGN-35 (Filed Mar 13), SYR-322/metformin (Filed Nov 13), SYR-322/pioglitazone (Filed Nov 13) |
| | Thailand | TAK-390MR (Approved Jun 13), TAK-491/chlorthalidone (Filed Jun 12), TCV-116/amlodipine besilate (Filed Aug 12), SYR-322/pioglitazone (Filed Mar 13), SGN-35 (Filed May 13), TAK-491 (Filed Dec 13), SYR-322 (Filed Feb 14), SYR-322/metformin (Filed Mar 14) |
| | Vietnam | roflumilast (Approved Apr 13) |
| Middle East, Oceania & Africa | Australia | SYR-322 (Approved Sep 13), SYR-322/metformin (Approved Oct 13), SGN-35 (Approved Dec 13), MLN0002 (Filed Jun 13), SYR-322/pioglitazone (Filed Apr 14) |
| | Egypt | roflumilast (Filed Jan 12), TAK-390MR (Filed Mar 13), TAK-491 (Filed Apr 13), TAK-491/chlorthalidone (Filed Jun 13), SYR-322 (Filed Jul 13), SYR-322/pioglitazone (Filed Aug 13), SYR-322/metformin (Filed Sep 13) |
| | Israel | SGN-35 (Filed Aug 13) |
| | Kenya | roflumilast (Approved Oct 13) |
| | Kuwait | TAK-491 (Filed Oct 13), TAK-491/chlorthalidone (Filed Oct 13) |
| | Oman | TAK-491 (Filed Oct 13), TAK-491/chlorthalidone (Filed Oct 13), TAK-390MR (Filed Oct 13) |
| | Qatar | TAK-491/chlorthalidone (Filed Nov 13), TAK-390MR (Filed Nov 13) |
| | South Africa | SGN-35 (Filed Jul 13), SYR-322 (Filed Dec 13), SYR-322/metformin (Filed Dec 13) |
| | UAE | TAK-491 (Approved Nov 13), TAK-390MR (Filed Jun 13), TAK-491/chlorthalidone (Filed Sep 13) |

*7 **TAK-491 <azilsartan medoxomil>** Angiotensin II receptor blocker (oral) for the treatment of Hypertension

*8 **TAK-375 <ramelteon>** MT1/MT2 receptor agonist (oral) for the treatment of insomnia

*9 **<roflumilast>** PDE4 inhibitor (oral) for the treatment of Chronic Obstructive Pulmonary Disease

*10 **<mifamurtide>** Immunostimulant (injection) for the treatment of Non-metastatic osteosarcoma

*11 **TCV-116 <candesartan cilexetil>** Angiotensin II receptor blocker (oral) for the treatment of Hypertension

## ■ Characteristics of projects

| Development Code <generic name> | Brand Name | Drug Class | Indications | Administration |
|---|---|---|---|---|
| **TAK-390MR <dexlansoprazole>** | DEXILANT® (US, Canada) DEXIVANT® (Mexico) | Proton pump inhibitor | Erosive esophagitis (healing and maintenance), Non-erosive gastro-esophageal reflux disease | Oral |
| [Mode of action / Supplemental] TAK-390MR was originally developed by Takeda and is launched in the US, Canada and Mexico, and has been appoved in 16 countries in the EU by the decentralized procedure. It is taken once-daily, and employs a new modified release technology on an enantiomer of lansoprazole. TAK-390MR is the first proton pump inhibitor with a Dual Delayed Release™ formulation designed to provide two separate releases of medication in order to maintain its gastric antisecretory activity. | | | | |

| Development Code <generic name> | Brand Name | Drug Class | Indications | Administration |
|---|---|---|---|---|
| **SYR-322 <alogliptin>** | NESINA® (Jpn, US) VIPIDIA® (EU) | DPP-4 inhibitor | Diabetes mellitus | Oral |
| [Mode of action / Supplemental] SYR-322 is a DPP-4 inhibitor, taken orally once a day. DPP-4 inhibitors work by blocking Glucagon Like Peptide-1 (GLP-1) degradation to maintain its blood concentration for a longer period of time. GLP-1, which is secreted within the digestive tract, stimulates pancreatic beta cells to increase the secretion of insulin, and GLP-1 has the potential to improve beta cell function itself. SYR-322 was approved in Japan in April 2010, in the US in January 2013, and in the EU in September 2013. Clinical/registration activities are currently ongoing in other regions to support the approval of SYR-322 globally. SYR-322 has also been approved in fixed-dose combinations with pioglitazone (in Japan as LIOVEL®, in the US as OSENI® and in the EU as INCRESYNC®), and metformin (in the US as KAZANO® and in the EU as VIPDOMET®). | | | | |

| Development Code <generic name> | Brand Name | Drug Class | Indications | Administration |
|---|---|---|---|---|
| **ATL-962 <cetilistat>** | OBLEAN® (Jpn) | Lipase inhibitor | Obesity with both type 2 diabetes mellitus and dyslipidemia | Oral |
| [Mode of action / Supplemental] ATL-962 is a gastro-intestinal lipase inhibitor, designed to decrease weight by reducing the digestion and thus the absorption of fat from the diet. In P-III trials, ATL-962 demonstrated a statistically significant greater reduction in bodyweight from baseline compared to placebo, with a good safety and tolerability profile. In September 2013, Takeda obtained marketing approval for ATL-962 from the Japanese Ministry of Health, Labour and Welfare. | | | | |

| Development Code <generic name> | Brand Name | Drug Class | Indications | Administration |
|---|---|---|---|---|
| **Lu AA21004 <vortioxetine>** | BRINTELLIX® (US) | Multimodal anti-depressant | Major depressive disorder, Generalized anxiety disorder | Oral |
| [Mode of action / Supplemental] Lu AA21004 is an inhibitor of serotonin (5-HT) reuptake and that is thought to be a mechanism of its action. It is also an agonist at 5-HT1A receptors, a partial agonist at 5-HT1B receptors and an antagonist at 5-HT3, 5-HT1D and 5-HT7 receptors. In vivo nonclinical studies have demonstrated that Lu AA21004 enhances levels of the neurotransmitters serotonin, noradrenaline, dopamine, acetylcholine and histamine in specific areas of the brain. In September 2013, Takeda obtained approval from the FDA for Lu AA21004 for the treatment of Major Depressive Disorder. | | | | |

| Development Code <generic name> | Brand Name | Drug Class | Indications | Administration |
|---|---|---|---|---|
| **SGN-35 <brentuximab vedotin>** | ADCETRIS® (EU, Jpn) | CD30 monoclonal antibody-drug conjugate | Relapsed or refractory Hodgkin lymphoma, Front line Hodgkin lymphoma, Post-ASCT Hodgkin lymphoma, Relapsed or refractory systemic anaplastic large cell lymphoma, Front line mature T-cell lymphoma, Relapsed cutaneous T-cell lymphoma | Injection |
| [Mode of action / Supplemental] SGN-35 is an antibody-drug conjugate (ADC) comprising an anti-CD30 monoclonal antibody attached by an enzyme cleavable linker to a potent, synthetic drug, monomethyl auristatin E (MMAE) utilizing Seattle Genetics' proprietary technology. The ADC employs a novel linker system that is designed to be stable in the bloodstream but to release MMAE upon internalization into CD30-expressing tumor cells. This approach is intended to spare non-targeted cells and thus may help minimize the potential toxic effects of traditional chemotherapy while allowing for the selective targeting of CD30-expressing cancer cells, thus potentially enhancing the antitumor activity. | | | | |

| Development Code <generic name> | Brand Name | Drug Class | Indications | Administration |
|---|---|---|---|---|
| **BLB-750** | Cell Culture Influenza vaccine (H5N1) "TAKEDA" 1mL<br>Cell Culture Influenza vaccine (Prototype) "TAKEDA" 1mL | Influenza vaccine | Prevention of pandemic influenza | Injection |
| [Mode of action / Supplemental]<br>BLB-750 is a cell culture-based pandemic influenza vaccine (H5N1 and prototype) to prevent infection in the case of a pandemic influenza. Obtaining the prototype approval will facilitate the registration of a vaccine in the event of a pandemic caused by an influenza strain other than H5N1. In March 2014, the Japanese Ministry of Health, Labour and Welfare approved the New Drug Application of Cell Cultured Influenza vaccine H5N1 "TAKEDA" 1mL and Cell Cultured Influenza vaccine (Prototype) "TAKEDA" 1mL for prevention of pandemic influenza to be manufactured in the Hikari Plant. | | | | |

| Development Code <generic name> | Brand Name | Drug Class | Indications | Administration |
|---|---|---|---|---|
| **<lurasidone hydrochloride>** | LATUDA® (EU) | Atypical antipsychotic agent | Schizophrenia, Bipolar disorder | Oral |
| [Mode of action / Supplemental]<br>Lurasidone is an atypical antipsychotic agent, developed originally by Dainippon Sumitomo Pharma Co., Ltd. with an affinity for dopamine D2, serotonin 5-$HT_{2A}$ and serotonin 5-$HT_7$ receptors where it has antagonist effects. In addition, lurasidone is a partial agonist at the serotonin 5-$HT_{1A}$ receptor and has no appreciable affinity for histamine or muscarinic receptors. In March 2014, lurasidone was approved in the EU for the treatment of schizophrenia. | | | | |

| Development Code <generic name> | Brand Name | Drug Class | Indications | Administration |
|---|---|---|---|---|
| **MLN0002 <vedolizumab>** | ENTYVIO™ (US, EU) | Humanized monoclonal antibody against α4β7 integrin | Ulcerative colitis, Crohn's disease | Injection |
| [Mode of action / Supplemental]<br>MLN0002 is a humanized monoclonal antibody that specifically antagonizes the α4β7 integrin, inhibiting the binding of α4β7 integrin to intestinal mucosal addressin cell adhesion molecule (MAdCAM-1). MAdCAM-1 is preferentially expressed on blood vessels and lymph nodes of the gastrointestinal tract. The α4β7 integrin is expressed on a subset of circulating white blood cells, and these cells have been shown to play a role in mediating the inflammatory process in ulcerative colitis and Crohn's disease. P-III studies have shown that MLN0002 demonstrates statistically significant improvement in clinical remission in patients with ulcerative colitis and Crohn's disease at 52 weeks versus placebo. In March 2013, Takeda filed a Marketing Authorisation Application in the EU for the treatment of ulcerative colitis and Crohn's disease, and in June 2013, Takeda filed a Biologics License Application (BLA) in the US for the same indications. | | | | |

| Development Code <generic name> | Brand Name | Drug Class | Indications | Administration |
|---|---|---|---|---|
| **TAK-438 <vonoprazan>** | Not decided yet | Potassium-competitive acid blocker | Acid-related diseases (GERD, Peptic ulcer, etc.) | Oral |
| [Mode of action / Supplemental]<br>TAK-438 is a potassium-competitive acid blocker (P-CAB) that suppresses gastric acid secretion by inhibiting the binding of potassium iron ($K^+$) to $H^+$, $K^+$-ATPase. It is anticipated to have a more potent inhibitory effect on gastric acid secretion, a faster onset of action, and a longer lasting effect than PPIs. In February 2014, Takeda filed a New Drug Application to Japanese Ministry of Health, Labour and Welfare. | | | | |

| Development Code <generic name> | Brand Name | Drug Class | Indications | Administration |
|---|---|---|---|---|
| **SYR-472 <trelagliptin>** | Not decided yet | DPP-4 inhibitor | Diabetes mellitus | Oral |
| [Mode of action / Supplemental]<br>SYR-472 is a DPP-4 inhibitor, taken orally once weekly, that works by blocking Glucagon Like Peptide-1 (GLP-1) degradation to keep its concentration for a longer period of time. GLP-1, which is secreted within the digestive tract, stimulates pancreatic beta cells to increase the secretion of insulin, and GLP-1 has the potential to improve beta cell function itself. In March 2014, Takeda filed a New Drug Application to Japanese Ministry of Health, Labour and Welfare. | | | | |

| Development Code <generic name> | Brand Name | Drug Class | Indications | Administration |
|---|---|---|---|---|
| **TAK-816** | Not decided yet | Hib vaccine | Prevention of infectious disease caused by Haemophilus influenza Type b (Hib) | Injection |
| [Mode of action / Supplemental]<br>TAK-816 is a vaccine to prevent infection caused by Haemophilus Influenza Type b (Hib). Hib vaccine is developed by combining it with detoxified diphtheria toxin in order to increase immunogenicity, assuring the potential to induce the production of antibodies in infants. In September 2013, Takeda filed a New Drug Application to Japanese Ministry of Health, Labour and Welfare for the prevention of infectious disease caused by Hib | | | | |

| Development Code <generic name> | Brand Name | Drug Class | Indications | Administration |
|---|---|---|---|---|
| **<naltrexone SR /bupropion SR>** | CONTRAVE® (US) | Mu-opioid receptor antagonist and dopamine/norepinephrine re-uptake inhibitor | Obesity | Oral |
| [Mode of action / Supplemental]<br>The two components of CONTRAVE act in a complementary manner in the central nervous system. The central pathways targeted by this treatment are involved in controlling the balance of food intake and metabolism, and regulating reward-based eating behavior. In clinical trials, CONTRAVE was shown to help obese patients initiate and sustain significant weight loss, improve important markers of cardiometabolic risk and increase the ability to control eating. | | | | |

| Development Code <generic name> | Brand Name | Drug Class | Indications | Administration |
|---|---|---|---|---|
| **<fomepizole>** | Not decided yet | Alcohol dehydrogenase inhibitor | Ethylene glycol and methanol poisonings | Injection |
| [Mode of action / Supplemental]<br>Fomepizole is an antidote to inhibit the metabolism of ethylene glycol and methanol by inhibiting alcohol dehydrogenase (ADH) competitively and thereby inhibiting production of toxic metabolites (organic acids). | | | | |

| Development Code <generic name> | Brand Name | Drug Class | Indications | Administration |
|---|---|---|---|---|
| **TAK-700 <orteronel>** | Not decided yet | Non-steroidal androgen synthesis inhibitor | Prostate cancer | Oral |
| [Mode of action / Supplemental]<br>TAK-700 is an oral non-steroidal selective androgen synthesis inhibitor which targets 17,20 lyase, a key enzyme in the production of steroidal hormones. The 17,20 lyase enzyme is a key enzyme in the production of the common precursor molecules for male and female sex steroid hormones, which in men are synthesized in both the testes and the adrenal glands. This inhibitory activity makes TAK-700 a good candidate for development as a therapeutic agent for the treatment of castration-resistant prostate cancer where persistent extra-gonadal synthesis of androgens results in progression of PSA and metastases. | | | | |

| Development Code <generic name> | Brand Name | Drug Class | Indications | Administration |
|---|---|---|---|---|
| **MLN9708 <ixazomib>** | Not decided yet | Proteasome inhibitor | Relapsed or refractory multiple myeloma, Previously untreated multiple myeloma, Relapsed or refractory primary (AL) amyloidosis, Solid tumors | Oral |
| [Mode of action / Supplemental]<br>MLN9708 is a proteasome inhibitor, which constitutes a unique approach to targeted therapy. Inhibition of the proteasome prevents the degradation of numerous regulatory proteins, affecting multiple signaling cascades within the cell. In vitro, non-clinical studies have shown that proteasome inhibition can be cytotoxic to a variety of cancer cell types. | | | | |

| Development Code <generic name> | Brand Name | Drug Class | Indications | Administration |
|---|---|---|---|---|
| **MLN8237 <alisertib>** | Not decided yet | Aurora A kinase inhibitor | Relapsed or refractory peripheral T-cell lymphoma, Small cell lung cancer, Ovarian cancer, Non-Hodgkin lymphoma, Solid tumors | Oral |
| [Mode of action / Supplemental]<br>MLN8237 is an oral highly-specific small molecule Aurora A kinase inhibitor. Both Aurora A kinase and Aurora B kinase play important roles in cell mitosis, but they have different distributions in the cell and different roles in the process of mitosis. Aurora A kinase is a serine/threonine kinase that exists in the centrosome and spindle poles and is known to play an important role in the formation of spindles at the time of mitosis. | | | | |

| Development Code <generic name> | Brand Name | Drug Class | Indications | Administration |
|---|---|---|---|---|
| **<motesanib diphosphate>** | Not decided yet | VEGFR1-3, PDGFR, c-Kit inhibitor | Advanced non-squamous non-small cell lung cancer | Oral |
| [Mode of action / Supplemental]<br>Motesanib is an orally administered inhibitor targeting vascular endothelial growth factor (VEGF) receptor 1,2 and 3, platelet derived growth factor (PDGF) receptor and c-kit (Stem Cell Factor) receptors intending to inhibit angiogenesis and tumor growth. | | | | |

| Development Code <generic name> | Brand Name | Drug Class | Indications | Administration |
|---|---|---|---|---|
| **AMG 386 <trebananib>** | Not decided yet | Anti-angiopoietin peptibody | Ovarian cancer | Injection |
| [Mode of action / Supplemental]<br>AMG 386 is a peptibody (Fc-peptide fusion protein) which binds to and inhibit Angiopoietin 1 and 2. Angiopoietins are known to be one of the cytokines which stimulate angiogenesis of vascular endothelial cells related to tumor growth and metastasis through different pathways from vascular endothelial growth factors (VEGF). AMG386 inhibits vascular angiogenesis through binding to angiopoietin 1 and 2. | | | | |

| Development Code <generic name> | Brand Name | Drug Class | Indications | Administration |
|---|---|---|---|---|
| **<peginesatide>** | OMONTYS® (US) | Synthetic, peptide-based erythropoiesis-stimulating agent | Anaemia associated with chronic kidney disease in adult patients undergoing dialysis | Injection |
| [Mode of action / Supplemental]<br>OMONTYS, a synthetic, peptide-based erythropoiesis-stimulating agent (ESA), is designed to stimulate the production of red blood cells. As PEGylation allows maintenance of blood concentration, peginesatide is administratered once every four weeks either intravenously or subcutaneously.<br>Serious cases of hypersensitivity reactions, including anaphylaxis, which can be life-threatening or fatal, were reported in the postmarketing setting in the US, leading to a voluntary recall of all lots of OMONTYS. An investigation into the root cause of the reactions was initiated and is ongoing. | | | | |

| Development Code <generic name> | Brand Name | Drug Class | Indications | Administration |
|---|---|---|---|---|
| **TAK-385 <relugolix>** | Not decided yet | LH-RH antagonist | Endometriosis, Uterine fibroids, Prostate cancer | Oral |
| [Mode of action / Supplemental]<br>TAK-385 is a nonpeptidic oral LH-RH antagonist. It antagonizes LH-RH in the LH-RH receptor that exists in the anterior pituitary basophil (secretory cell), and lowers blood concentration of sex hormones by inhibiting secretion of LH and FSH caused by the stimulation of LH-RH. It is expected to become a treatment for sex hormone-dependent diseases such as endometriosis and uterine fibroids. | | | | |

| Development Code <generic name> | Brand Name | Drug Class | Indications | Administration |
|---|---|---|---|---|
| **MLN0128** | Not decided yet | mTORC1/2 inhibitor | Breast cancer, Solid tumors | Oral |
| [Mode of action / Supplemental]<br>MLN0128, a novel mTORC1/2 inhibitor, has generated encouraging data in multiple P-I studies and entered P-II studies for breast cancer in 2014. | | | | |

| Development Code <generic name> | Brand Name | Drug Class | Indications | Administration |
|---|---|---|---|---|
| **TAK-003** | Not decided yet | Tetravalent Dengue vaccine | Prevention of dengue fever caused by dengue virus | Injection |
| [Mode of action / Supplemental]<br>Takeda's tetravalent Dengue vaccine candidate is a live virus (attenuated tetravalent) vaccine, including the four serotypes of the dengue virus. The chimeric, attenuated vaccine strains for dengue serotypes 1, 3 and 4 were engineered by replacing the DEN-2 PDK-53 structural genes, premembrane (prM) and envelope (E), with the prM and E genes of the respective wt virus strains that cause disease in humans. In preclinical models, this candidate stimulates both types of acquired immunity: humoral (antibody) and cell-mediated (T-cell) immune responses. In early Phase--I and Phase-II clinical studies, Takeda's Tetravalent Dengue Vaccine Candidate induced immune responses in all of the dengue virus serotypes after two vaccinations with no safety concerns. | | | | |

| Development Code <generic name> | Brand Name | Drug Class | Indications | Administration |
|---|---|---|---|---|
| **Norovirus vaccine** | Not decided yet | Norovirus vaccine | Prevention of acute gastroenteritis (AGE) caused by norovirus | Injection |
| [Mode of action / Supplemental]<br>The norovoris vaccine includes virus-like particle (VLP) antigens representing each of the two genogroups that predominantly cause illness in humans, and is formulated with alum and MPL adjuvants. Takeda's product candidate is the only clinical-stage vaccine against norovirus in the world. Phase I and I/II studies showed the vaccine to be generally well tolerated, and a reduction in mild, moderate or severe vomiting and diarrhea symptoms was demonstrated in vaccinees upon oral challenge with live norovirus. The norovirus vaccine is administered by the intramuscular route. | | | | |

| Development Code <generic name> | Brand Name | Drug Class | Indications | Administration |
|---|---|---|---|---|
| **TAK-114** | Not decided yet | Pro-inflammatory cytokine inhibitor | Ulcerative colitis | Oral |
| [Mode of action / Supplemental]<br>TAK-114 is a synthetic small molecule that is believed to inhibit expression of pro-inflammatory cytokines (IL-1β, IL-6, IL-12 and TNF-α), which can increase inflammation and worsen the disease, and stimulate expression of a cytokine (IL-10) which further suppresses pro-inflammatory responses. These anti-inflammatory responses may limit unnecessary tissue disruptions caused by inflammation. | | | | |

| Development Code <generic name> | Brand Name | Drug Class | Indications | Administration |
|---|---|---|---|---|
| **TAK-361S** | Not decided yet | Tetravalent vaccine | Prevention of infectious disease caused by Diphtheria, Pertussis, Tetanus, Poliomyelitis | Injection |
| [Mode of action / Supplemental]<br>TAK-361S is a combined vaccine with a Diphtheria-Tetanus-acellular Pertussis (DTaP) vaccine and Sabin inactivated polio vaccine (sIPV). sIPV is an inactivated poliovirus vaccine (IPV) derived from the Sabin strains poliovirus (attenuated poliovirus). Compared to the inactivated poliovirus vaccine produced from wild-type poliovirus that is used in many countries, sIPV does not require an advanced safe management site for its production. | | | | |

| Development Code <generic name> | Brand Name | Drug Class | Indications | Administration |
|---|---|---|---|---|
| **MT203 <namilumab>** | Not decided yet | GM-CSF monoclonal antibody | Psoriasis, Rheumatoid arthritis | Injection |
| [Mode of action / Supplemental]<br>MT203 works by neutralizing GM-CSF (a fully human monoclonal antibody neutralizing Granulocyte macrophage colony-stimulating factor) signaling by binding the soluble cytokine. GM-CSF, a pro-inflammatory cytokine, has been shown to play a significant role in various autoimmune and inflammatory disease and supports development of MT203 for the treatment of psoriasis and rheumatoid arthritis (RA). | | | | |

| Development Code <generic name> | Brand Name | Drug Class | Indications | Administration |
|---|---|---|---|---|
| **TAK-850** | Not decided yet | Influenza vaccine | Prevention of influenza disease caused by influenza virus subtype A and B contained in the vaccine | Injection |
| [Mode of action / Supplemental]<br>TAK-850 is an inactivated, cell-culture seasonal influenza vaccine based on Baxter's Vero cell culture technology. It is expected to be suitable for people with allergies because of the absence of eggs, preservatives, adjuvant or antibiotics. | | | | |

| Development Code <generic name> | Brand Name | Drug Class | Indications | Administration |
|---|---|---|---|---|
| **TAK-733** | Not decided yet | MEK inhibitor | Solid tumors | Oral |
| [Mode of action / Supplemental]<br>TAK-733 is a highly selective, allosteric, non-ATP competitive inhibitor of MEK kinase. MEK signaling plays an essential role in regulating both mitogenic and survival signals within tumor cells. This pathway is activated in 50 percent of human cancers, including colon, lung, breast, pancreas, melanoma, ovary and kidney. Inhibition of MEK by TAK-733 as a single agent and in combination with other drugs has a significant effect on the progression of tumor growth in pre-clinical models. | | | | |

| Development Code <generic name> | Brand Name | Drug Class | Indications | Administration |
|---|---|---|---|---|
| **TAK-272** | Not decided yet | Direct renin inhibitor | Hypertension | Oral |
| [Mode of action / Supplemental]<br>TAK-272 is a direct renin inhibitor (DRI), which is at the top of the enzymatic cascade of renin-angiotensin system (RAS). Non-clinical pharmacology studies have shown that TAK-272 selectively inhibited human renin and efficiently lowered blood pressure. Additionally TAK-272 has shown strong organ protective effects. | | | | |

| Development Code <generic name> | Brand Name | Drug Class | Indications | Administration |
|---|---|---|---|---|
| **TAK-063** | Not decided yet | PDE10A inhibitor | Schizophrenia | Oral |
| [Mode of action / Supplemental]<br>TAK-063 is a PDE10A inhibitor. An alternative approach to treating schizophrenia may be to selectively inhibit the enzyme PDE10A, thereby modulating the dopaminergic and glutamatergic second messenger pathways in the striatum. Inhibition of PDE10A in vivo has been reported to be associated with behavioral effects consistent with antipsychotic activity. Based on the potential effects of TAK-063 on striatal function, the initial nonclinical and clinical programs for TAK-063 are focused on the treatment of schizophrenia. | | | | |

| Development Code <generic name> | Brand Name | Drug Class | Indications | Administration |
|---|---|---|---|---|
| **TAK-137** | Not decided yet | AMPA receptor potentiator | Psychiatric disorders and neurological diseases | Oral |
| [Mode of action / Supplemental]<br>TAK-137 is an AMPA receptor (AMPA-R) potentiator. Glutamate is the major excitatory neurotransmitter in the brain and it produces its effects by binding to different receptors such as the AMPA (α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid)-type glutamate receptor. In fact, AMPA receptors mediate most of the excitatory neurotransmission in the human central nervous system and are also involved in processes thought to underlie memory and learning, and the formation of neural networks during brain development. Published preclinical and clinical data have suggested that positive modulation of AMPA receptors may be therapeutically effective in the treatment of various psychiatric disorders and neurological diseases. Of particular interest is the potential for AMPA-R potentiators to ameliorate cognitive deficits, a symptom known to accompany many CNS conditions. | | | | |

| Development Code <generic name> | Brand Name | Drug Class | Indications | Administration |
|---|---|---|---|---|
| **TAK-659** | Not decided yet | SYK kinase inhibitor | Solid tumors, Hematologic malignancies | Oral |
| [Mode of action / Supplemental]<br>TAK-659 is an orally bioavailable, selective inhibitor of SYK (Spleen Tyrosine Kinase) and FLT3 (FMS-like tyrosine kinase-3). SYK is a non-receptor protein tyrosine kinase that is widely expressed in hematopoietic cells. It is involved in coupling activated immuno-receptors (B-cell and Fc receptors) to downstream signaling events that mediate diverse cellular responses including proliferation, differentiation and phagocytosis. SYK is known to be activated in lymphomas and leukemias. Tumor populations enriched for activated SYK expression include B-cell tumors that require signaling through BcR, myeloid tumors that signal through FcgR and EBV-associated heme and solid tumor malignancies. | | | | |

| Development Code <generic name> | Brand Name | Drug Class | Indications | Administration |
|---|---|---|---|---|
| **TAK-233** | Not decided yet | - | - | Oral |
| [Mode of action / Supplemental]<br>TAK-233 is a novel and orally available drug. | | | | |

| Development Code <generic name> | Brand Name | Drug Class | Indications | Administration |
|---|---|---|---|---|
| **INV21** | Not decided yet | EV71 vaccine | Prevention of hand, foot and mouth disease caused by enterovirus 71 | Injection |
| [Mode of action / Supplemental]<br>INV21 is an inactivated whole virus particle formulated with aluminum hydroxide adjuvant, produced in Vero cells. The vaccine is based on a common strain of EV71 (the B2 sub-genogroup). In a P-I study in 36 healthy adults in Singapore, INV21 induced robust, neutralizing antibody responses against the EV71 virus in every individual. There were no safety concerns in the trial. | | | | |

| Development Code <generic name> | Brand Name | Drug Class | Indications | Administration |
|---|---|---|---|---|
| **MLN4924** | Not decided yet | NEDD 8 activating enzyme inhibitor | Advanced malignancies | Injection |

[Mode of action / Supplemental]
MLN4924 is a first-in-class small molecule inhibitor of a Millennium-discovered target, NEDD 8 activating enzyme (NAE). MLN4924 inhibits NAE, which controls key components of the ubiquitin proteasome pathway that are important for cancer cell growth and survival. In pre-clinical models, MLN4924 suppresses cancer cell growth leading to cell death. MLN4924 is currently being studied in patients with solid tumors and hematologic malignancies.

| Development Code <generic name> | Brand Name | Drug Class | Indications | Administration |
|---|---|---|---|---|
| **MLN1117** | Not decided yet | PI3Kalpha isoform inhibitor | Solid tumors | Oral |

[Mode of action / Supplemental]
MLN1117, a novel and selective inhibitor of the PI3Kalpha isoform, entered human clinical testing in September 2011. A P-I dose escalation study is underway to evaluate the safety, tolerability and pharmacokinetics of single-agent MLN1117 in patients with advanced solid malignancies who have tumors characterized by the presence of a PIK3CA mutation.

| Development Code <generic name> | Brand Name | Drug Class | Indications | Administration |
|---|---|---|---|---|
| **MLN0264** | Not decided yet | Antibody-drug conjugate targeting GCC | Advanced gastrointestinal malignancies | Injection |

[Mode of action / Supplemental]
MLN0264 is a novel, first in class antibody drug conjugate (ADC) that selectively binds Guanylate Cyclase C (GCC) and kills GCC-expressing cells at sub-nanomolar concentrations. Its toxic payload, monomethyl auristatin E (MMAE; a very potent microtubulin inhibitor) is linked to a target specific monoclonal antibody (developed by Millennium), via a cleavable linker (utilizing proprietary technology licensed from Seattle Genetics).
GCC is a transmembrane receptor localized on the apical, but not the basolateral, membrane of epithelial tissues primarily in the gastrointestinal (GI) tract. Malignant transformation results in loss of this anatomically privileged GCC expression profile and tumor, but not normal, tissue becomes accessible to systemically administered agents targeting GCC. GCC is expressed across various cancers, including gastric, pancreatic and colorectal cancer.

| Development Code <generic name> | Brand Name | Drug Class | Indications | Administration |
|---|---|---|---|---|
| **MLN7243** | Not decided yet | UAE Inhibitor | Solid tumors | Injection |

[Mode of action / Supplemental]
MLN7243 is a first-in-class selective inhibitor of Ubiquitin Activating Enzyme（UAE）. MLN7243 inhibits UAE driven ubiquitination resulting in ER (Endoplasmic Reticulum) stress, defective DNA repair, cell cycle arrest and apoptosis.

| Development Code <generic name> | Brand Name | Drug Class | Indications | Administration |
|---|---|---|---|---|
| **MLN2480** | Not decided yet | pan-Raf kinase inhibitor | Solid tumors | Oral |

[Mode of action / Supplemental]
MLN2480 is a selective pan-Raf kinase inhibitor. The Raf kinases (A-Raf, B-Raf and C-Raf) are key regulators of cell proliferation and survival within the mitogen-activated protein kinase (MAPK) pathway. The MAPK pathway is frequently disregulated in human cancers, often via activating mutations of Ras or Raf. Following treatment with MLN2480, significant antitumor activity was observed in both tumor xenograft models that had B-Raf$^{V600E/D}$ mutations or were wild type for B-Raf. MLN2480 exhibited a promising preclinical profile and has potential to be a therapeutic agent for solid tumors.

| Development Code <generic name> | Brand Name | Drug Class | Indications | Administration |
|---|---|---|---|---|
| **ITI-214** | Not decided yet | PDE1 inhibitor | Cognitive impairment associated with schizophrenia | Oral |

[Mode of action / Supplemental]
ITI-214 potently inhibits the phosphodiesterase1 (PDE1) enzyme. The PDE1 inhibitor mechanism amplifies dopamine D1 receptor signaling in the prefrontal cortex of the brain, leading to improvement of cognition. This is unique compared to typical drugs for schizophrenia, most of which directly work on blocking dopamine receptors. PDE1 inhibitors including ITI-214 have been shown to enhance cognition in preclinical models.

| Development Code <generic name> | Brand Name | Drug Class | Indications | Administration |
|---|---|---|---|---|
| **Lu AA24530** | Not decided yet | Multimodal anti-depressant | Major depressive disorder, Generalized anxiety disorders | Oral |
| [Mode of action / Supplemental]<br>In pre-clinical studies, Lu AA24530 has demonstrated activities as a multi-modal enhancer with reuptake inhibition at monoamine transporters, and antagonist activity at 5-$HT_3$ and 5-$HT_{2c}$ receptors. In vivo rat studies have demonstrated that treatment with Lu AA24530 leads to increases in acetylcholine, noradrenaline, dopamine and 5-HT levels in brain regions that play a key role in the regulation of mood. | | | | |

| Development Code <generic name> | Brand Name | Drug Class | Indications | Administration |
|---|---|---|---|---|
| **AMG 403 <fulranumab>** | Not decided yet | Human monoclonal antibody against human Nerve Growth Factor (NGF) | Pain | Injection |
| [Mode of action / Supplemental]<br>AMG 403 is a human monoclonal antibody that has the specific capacity to neutralize the biologic actions of human NGF. NGF has been shown to contribute to persistent pain in a variety of animal models of inflammatory and neuropathic pain, and is known to be elevated in the knee joints of humans with chronic arthritis and possibly other chronic painful conditions in humans. | | | | |

| Development Code <generic name> | Brand Name | Drug Class | Indications | Administration |
|---|---|---|---|---|
| **<rasagiline>** | Not decided yet | Monoamine oxidase B (MAO-B) inhibitor | Parkinson's disease | Oral |
| [Mode of action / Supplemental]<br>Rasagiline is an innovative treatment for Parkinson's disease, and Takeda has signed an agreement with Teva allowing Takeda to commercialize it in Japan. Rasagiline is a monoamine oxidase B (MAO-B) inhibitor which is presumed to act by increasing available synaptic dopamine in the brain which may improve the motor symptoms characteristic of Parkinson’s disease. | | | | |

| Development Code <generic name> | Brand Name | Drug Class | Indications | Administration |
|---|---|---|---|---|
| **TAK-491 <azilsartan medoxomil>** | EDARBI® (EU) | Angiotensin II receptor blocker | Hypertension | Oral |
| [Mode of action / Supplemental]<br>TAK-491 is an angiotensin II receptor blocker, indicated for the treatment of hypertension, either alone or in combination with other antihypertensive agents. Pivotal P-III studies of monotherapy showed TAK-491 80mg was statistically superior to placebo and the highest approved doses of olmesartan medoxomil (40mg) and valsartan (320mg), in lowering both clinic and 24-hour mean blood pressure measurements. | | | | |

| Development Code <generic name> | Brand Name | Drug Class | Indications | Administration |
|---|---|---|---|---|
| **<roflumilast>** | DAXAS® (EU) | PDE-4 inhibitor | Chronic Obstructive Pulmonary Disease | Oral |
| [Mode of action / Supplemental]<br>DAXAS is a first-in-class, once-daily orally administered selective phosphodiesterase 4 (PDE4) inhibitor. It is a non-steroid, anti-inflammatory agent designed to target both the systemic and pulmonary inflammation associated with COPD. The mechanism of action is the inhibition of PDE4, a major cyclic adenosine monophosphate (cAMP)-metabolising enzyme found in structural and inflammatory cells important to the pathogenesis of COPD. Inhibition of PDE4 increases intracellular cAMP and typically leads to an anti-inflammatory effect. | | | | |

| Development Code <generic name> | Brand Name | Drug Class | Indications | Administration |
|---|---|---|---|---|
| **<mifamurtide>** | MEPACT® (EU) | Immunostimulant | Non-metastatic osteosarcoma | Injection |
| [Mode of action / Supplemental]<br>MEPACT is a first-in-class synthetic analog of muramyl dipeptide (MDP). MEPACT is a liposomal formulation specifically designed for in vivo targeting to macrophages by intravenous infusion. | | | | |

| Development Code <generic name> | Brand Name | Drug Class | Indications | Administration |
|---|---|---|---|---|
| **TCV-116 <candesartan cilexetil>** | BLOPRESS® (Jpn, EU) | Angiotensin II receptor blocker | Hypertension | Oral |
| [Mode of action / Supplemental]<br>TCV-116 lowers blood pressure by suppressing the effect of angiotensin II, a hypertensive hormone, at the receptor level. | | | | |

## [Additional indications/formulations]

| Development Code <generic name> | Brand Name | Drug Class | Additional indications/formulations | Administration |
|---|---|---|---|---|
| **AG-1749 <lansoprazole>** | TAKEPRON® (Jpn), PREVACID® (US), OGAST® (EU) | Proton pump inhibitor | Fixed-dose combination with low-dose aspirin | Oral |
| [Mode of action / Supplemental]<br>AG-1749 is a proton pump inhibitor having a potent inhibitory action on gastric secretion. It suppresses gastric acid secretion by inhibiting the proton pump within the gastric wall cells and exhibits an antiulcer action. The drug has already been launched as a therapeutic agent for peptic ulcers in approximately 90 countries worldwide. The fixed-dose combination with low-dose aspirin was approved in Japan in March 2014 with the brand name TAKELDA®. | | | | |

| Development Code <generic name> | Brand Name | Drug Class | Additional indications/formulations | Administration |
|---|---|---|---|---|
| **TAK-536 <azilsartan>** | AZILVA® (Jpn) | Angiotensin II receptor blocker | Hypertension | Oral |
| [Mode of action / Supplemental]<br>The P-III trial in comparison with candesartan (BLOPRESS®) showed that TAK-536 was statistically superior to candesartan in lowering the change from baseline in sitting diastolic blood pressure, which was the primary endpoint. In addition, TAK-536 was also statistically superior to candesartan in lowering the change from baseline in sitting systolic blood pressure and in lowering the mean diastolic blood pressure and systolic blood pressure in 24 hours, daytime and night time measured by Ambulatory Blood Pressure Monitoring (ABPM), which were secondary endpoints. TAK-536 was safe and well tolerated, with the safety profile comparable to candesartan. The fixed-dose combination with amlodipine was approved in Japan in March 2014 with the brand name ZACRAS®. | | | | |

| Development Code <generic name> | Brand Name | Drug Class | Additional indications/formulations | Administration |
|---|---|---|---|---|
| **<ferumoxytol>** | RIENSO® (EU), FERAHEME® (Canada) | IV iron | Iron deficiency anemia from all causes in patients who have a history of unsatisfactory oral iron therapy or in whom oral iron cannot be used | Injection |
| [Mode of action / Supplemental]<br>Treatment with RIENSO provides the following benefits: rapid repletion of iron stores in anemic patients; greater flexibility in the amount of iron that can be given to a patient in a single administration; fewer physician visits required for the administration of 1g of iron; and more rapid administration (IV vs. infusion) compared to existing formulations of IV iron. RIENSO was approved for iron deficiency anemia in adult patients with chronic kidney disease in the EU in June 2012, and is currently under review for iron deficiency anemia from all causes in patients who have a history of unsatisfactory oral iron therapy or in whom oral iron cannot be used. The product is also approved in Canada, where it is marketed by Takeda as FERAHEME, and in the US, where it is marketed by AMAG. | | | | |

| Development Code <generic name> | Brand Name | Drug Class | Additional indications/formulations | Administration |
|---|---|---|---|---|
| **TAP-144-SR <leuprorelin acetate>** | LEUPLIN® (Jpn), LUPRON DEPOT® (US), ENANTONE®, etc. (EU, Asia) | LH-RH agonist | Prostate cancer, Premenopausal breast cancer (6-month formulation) | Injection |
| [Mode of action / Supplemental]<br>TAP-144-SR is a long-acting LH-RH agonist product, and is marketed in over 80 countries world-wide. It is a standard treatment of prostate cancer, and wth one injection it is possible to provide treatment from one to six months in the EU. A 3-month formulation was authorized in Japan for prostate cancer in August 2002 and for premenopausal breast cancer in August 2005. A 6-month formulation has been approved in the EU and has entered P-III in Japan. | | | | |

| Development Code <generic name> | Brand Name | Drug Class | Additional indications/formulations | Administration |
|---|---|---|---|---|
| **TAK-375SL <ramelteon>** | ROZEREM® (US, Jpn) | $MT_1/MT_2$ receptor agonist | Bipolar disorder | Sublingual |
| [Mode of action / Supplemental]<br>TAK-375SL is highly specific to the $MT_1/MT_2$ receptor. Abnormalities on circadian rhythms are prominent features of bipolar I disorder. Normalization or resynchronization of circadian rhythms with exogenous melatonin agonists is expected to become a treatment for either acute bipolar episodes or to prevent recurrence. | | | | |

| Development Code <generic name> | Brand Name | Drug Class | Additional indications/formulations | Administration |
|---|---|---|---|---|
| **<bortezomib>** | VELCADE® | Proteasome inhibitor | Front line mantle cell lymphoma,<br>Relapsed diffuse large B-cell lymphoma | Injection |
| [Mode of action / Supplemental]<br>VELCADE blocks the activity of proteasomes, which are enzymes found inside all human cells and necessary for their growth and survival. By inhibiting proteasomes activity, VELCADE causes a buildup of proteins, thereby inducing apoptosis/cell death. Proteasomes break down the resultant proteins which are created through the division and growth of cancer cells as well as other misfolded intracellular proteins. Proteasomes also break down the proteins that are responsible for angiogenesis and cell proliferation. | | | | |

| Development Code <generic name> | Brand Name | Drug Class | Additional indications/formulations | Administration |
|---|---|---|---|---|
| **AD-4833/TOMM40** | - | Insulin sensitizer/<br>Biomarker assay | Delay of onset of mild cognitive impairment due to Alzheimer's disease | Oral |
| [Mode of action / Supplemental]<br>The TOMM40 biomarker, discovered by Zinfandel, together with APOE and age, is being developed to identify older adults at high risk of developing mild cognitive impairment due to Alzheimer's disease within the subsequent five years. In August 2013, Takeda and Zinfandel initiated a global P-III clinical trial (TOMMORROW Trial) investigating a genetic based biomarker risk assignment algorithm utilizing TOMM40 to predict risk of mild cognitive impairment (MCI) due to Alzheimer's disease (AD) within a five year period. The TOMMORROW trial will also evaluate the efficacy of the investigational low dose AD-4833 (pioglitazone) in delaying the onset of MCI due to AD in cognitively normal individuals at high risk as determined by the risk assignment algorithm | | | | |

| Development Code <generic name> | Brand Name | Drug Class | Additional indications/formulations | Administration |
|---|---|---|---|---|
| **<lubiprostone>** | AMITIZA® (US) | Chloride channel activator | Liquid formulation, Pediatric functional constipation | Oral |
| [Mode of action / Supplemental]<br>Amitiza has a novel mechanism of action as a chloride channel activator, which causes an increase in intestinal fluid secretion, thereby increasing the passage of the stool and additionally stimulates recovery of mucosal barrier function and reduces intestinal permeability via the restoration of tight junction protein complexes, improving symptoms associated with chronic idiopathic constipation (CIC), irritable bowel syndrome with constipation (IBS-C) and opioid-induced constipation (OIC). | | | | |

| Development Code <generic name> | Brand Name | Drug Class | Additional indications/formulations | Administration |
|---|---|---|---|---|
| **TMX-67XR <febuxostat>** | ULORIC® (US) | Non-purine, selective xanthine oxidase inhibitor | Extended release formulation | Oral |
| [Mode of action / Supplemental]<br>Febuxostat is a non-purine selective inhibitor of xanthine oxidase which causes gout, maketed by Takeda in the U.S. as ULORIC. An extended release formulation is in development. | | | | |

## ■ Other alliance projects

| | | | | |
|---|---|---|---|---|
| **TAK-799/TRM-1** | **Licensed from:**<br>**Human Genome Sciences, Inc.** | **Agreed:** | Aug 2002 | |
| | | **Stage:** | Under preparation for clinical trials (Japan) | **Territory: Japan** |
| A complete human antibody relevant to TRAIL-R1 discovered by Human Genome Sciences, Inc. HGS is conducting P-II studies for multiple myeloma and non-squamous non-small cell lung cancer in the US. | | | | |

| | | | | |
|---|---|---|---|---|
| **Kanda HPV vaccine** | **Licensed from:**<br>**The Japan Health Sciences Foundation** | **Agreed:** | October 2010 | |
| | | **Stage:** | Under preparation for clinical trials | **Territory : Worldwide** |
| Kanda human papillomavirus (HPV) vaccine has the potential to be effective against all 15 high-risk HPV that are highly likely to cause cervical cancer. Since the coverage of high-risk HPV by conventional vaccines is not yet sufficient, Kanda HPV has the potential to become a universal vaccine. So far, it has been confirmed that the Kanda HPV vaccine has neutralizing activity against six variations of high-risk HPV that are often identified in cervical cancer patients. | | | | |

## ■ Clinical study protocol summaries

All clinical study protocol summaries are disclosed on the English-language web-site (http://www.takeda.com/c-t/) and all clinical study protocol information in the Japanese-language is disclosed on the Japanese-language web-site (http://www.takeda.co.jp/c-t/).

We anticipate that this disclosure assure transparency of information on the clinical trials for the benefit of healthcare professionals, their patients and other stakeholders, which we believe will contribute to the appropriate use of Takeda's products worldwide.

## ■ Outcome studies

### SYR-322 (1)

| Study title | EXAMINE (EXamination of cArdiovascular outcoMes: alogliptIN vs. standard of carE) | | |
|---|---|---|---|
| **Outline** | A Multicenter, Randomized, Double-Blind, Placebo-Controlled Study to Evaluate Cardiovascular Outcomes Following Treatment with Alogliptin in Addition to Standard of Care in Subjects with Type 2 Diabetes and Acute Coronary Syndrome | | |
| **Place** | 918 locations globally | **Total population** | 5,384 patients |
| **Status** | The EXAMINE CV safety outcomes trial met its primary endpoint of non-inferiority compared to placebo in addition to standard of care showing that alogliptin does not increase CV risk in Type 2 diabetes patients at high-risk for MACE due to recent ACS. The EXAMINE trial primary endpoint occurred at similar rates in the alogliptin and placebo groups (in 11.3% of patients vs. 11.8% of patients during a median follow-up period of 18 months; hazard ratio, 0.96; one-sided repeated CI, 1.16).<br><br>The principal secondary safety endpoint was the primary composite with the addition of hospitalization for unstable angina that required coronary revascularization within 24 hours of hospital admission. Testing of the secondary composite endpoint of CV death, myocardial infarction, stroke and unstable angina with urgent revascularization showed no difference in rates on alogliptin versus placebo (12.7% vs. 13.4%, hazard ratio, 0.95, one-sided repeated CI bound, 1.14).<br><br>Other secondary endpoints included CV death alone and death from any cause. CV death, occurred in 112 patients treated with alogliptin (4.1%) and 130 patients treated with placebo (4.9%) for a hazard ratio of 0.85 (95% confidence limits [CL] of 0.66 to 1.10, p = 0.21). All cause mortality (death from any cause) occurred in 153 patients treated with alogliptin (5.7%) and 173 patients treated with placebo (6.5%) for a hazard ratio of 0.88 (95% CL of 0.71 to 1.09, p = 0.23). Overall, rates of death from any cause and CV death were not statistically significant different between alogliptin and placebo groups.<br><br>Additional safety end points included angioedema, hypoglycemia, pancreatitis, malignancy, and results of laboratory testing. Rates of hypoglycemia, malignancy, pancreatitis, dialysis, and serum aminotransferase elevations were similar for the alogliptin and placebo groups. No events of pancreatic cancer were reported during the trial. The alogliptin and placebo groups did not differ significantly with regard to rates of serious adverse events (33.6% and 35.5%, respectively, p = 0.14). | | |

### AD-4833 (1)

| Study title | PROactive (PROspective pioglitAzone Clinical Trial In macroVascular Events) | | |
|---|---|---|---|
| **Outline** | This is a study to investigate the preventive effects on the progression of macrovascular disease in type 2 diabetes patients.<br>AD-4833 or placebo will be added to conventional oral anti-diabetic drugs for comparative purpose. Primary endpoints are cardiovascular events (death, heart attack, stroke, and below-knee amputation). | | |
| **Place** | 19 countries in Europe | **Total population** | 5,238 patients |
| **Status** | Landmark data from the PROactive Study, presented at the 41st meeting of the European Association for the Study of Diabetes (EASD) in Athens (Sep 05) demonstrated that ACTOS® (pioglitazone HCl) significantly reduces the combined risk of heart attacks, strokes and death by 16% in high risk patients with type 2 diabetes. This study focused on two key endpoints: a primary combination endpoint of seven different macrovascular events of varying clinical importance; and a principal secondary combination endpoint of life-threatening events including death, heart attack and stroke. The study results were published in The Lancet in October 2005.<br>The primary endpoint was reduced by 10% but had not reached statistical significance by study end (P=0.095). The principal secondary endpoint of life-threatening events showed that pioglitazone significantly reduced the risk of heart attacks, strokes and death by 16% (P=0.027).<br>Results of new analyses found that ACTOS (pioglitazone HCl) significantly reduced the risk of recurrent stroke in high-risk patients with type 2 diabetes at the World Congress of Cardiology in Barcelona. According to the results, there were statistically significant benefits of ACTOS in patients who had suffered a prior stroke. The incidence of recurrent stroke was reduced by 47 percent (P=0.008) and the combined risk of death, MI or stroke was reduced by 28 percent (P<0.05).<br>There was no effect of ACTOS on subsequent strokes in patients who had never experienced a stroke. | | |

### AD-4833 (2)

| Study title | CHICAGO (Carotid intima-media tHICkness in Atherosclerosis using pioGlitazOne) | | |
|---|---|---|---|
| **Outline** | CHICAGO is the largest and longest study to examine the effects of ACTOS on measures of the atherosclerotic disease process in patients with type 2 diabetes, by carotid intima-media thickness, or CIMT, that is defined as the thickness of the inner lining of a patient's carotid, or neck artery. | | |
| **Place** | US | **Total population** | 462 patients |
| **Status** | Results from the clinical trial, CHICAGO were part of a late-breaker presentation at the American Heart Association's Scientific Sessions 2006. The study results were published in the JAMA (the Journal of the American Medical Association) in November 2006.<br><br>The analysis demonstrated a statistically significant relative reduction in the progression of CIMT with ACTOS. According to the results, patients in the ACTOS arm showed a -0.001 mm change in arterial thickness from baseline versus an increase of 0.012 mm in the glimepiride arm, a total difference of 0.013 mm between the two arms (P=0.017). The results also showed a highly significant relative change in the maximum CIMT values, commonly considered a more indicative measure of overall treatment impact. The glimepiride-treated group showed a 0.026 increase, compared to a 0.002 increase in the ACTOS-treated group, resulting in a treatment difference of 0.024 (P=0.008).<br><br>ACTOS provided significantly better glycemic control based on reductions in A1c levels, which in the ACTOS-treated group decreased by 0.33 percent versus the glimepiride group that saw a decrease of 0.01 percent, resulting in a -0.32 percent (P=0.002) difference between the two arms.<br><br>Adjudicated cardiac events, composite endpoints of non-fatal myocardial infarction (MI), non-fatal stroke and death, showed no events in the ACTOS arm (n=230) and 2 events in the glimepiride arm (n=228).<br><br>ACTOS decreased triglyceride levels by 13.5 percent versus an increase of 2.1 percent with glimepiride (P=0.001), and increased HDL-C levels by 12.8 percent versus a decrease of 1.1 percent with glimepiride (P=0.001). Both treatment arms increased in LDL-C levels: 5.8 percent with ACTOS compared to 1 percent with glimepiride (P=0.12). | | |

## AD-4833 (3)

| Study title | PERISCOPE (Pioglitazone Effect on Regression of Intravascular Sonographic Coronary Obstruction Prospective Evaluation) | | |
|---|---|---|---|
| **Outline** | PERISCOPE is the first clinical trial to examine the effects of an oral antidiabetic medication on the development of coronary atherosclerosis in patients with type 2 diabetes using IVUS technology. | | |
| **Place** | US, Canada, Latin America | **Total population** | 543 patients |
| **Status** | The PERISCOPE trial was presented as a late breaker at the 57th Annual Scientific Session of the American College of Cardiology in Chicago in 2008. This trial demonstrated that ACTOS slows progression and reductions in atheroma volume which is a marker of coronary atherosclerosis. This trial adds to the body of cardiovascular data for ACTOS. ACTOS studies, conducted over the past 10 years in more than 16,000 patients, including short- and long-term trials, as well as prospective and observational studies, have shown no evidence that ACTOS is associated with an increased risk of heart attack, stroke, or death. The study results were published in the JAMA (the Journal of the American Medical Association) in March 2008.<br><br>The analysis demonstrated a statistically significant difference in percent change in coronary artery atheroma volume in favor of ACTOS treatment compared to glimepiride treatment. The data showed that patients treated with glimepiride, a sulfonylurea and commonly used diabetes medication, exhibited progression of coronary atherosclerosis. In contrast, the ACTOS arm showed no progression of coronary atherosclerosis over the 18-month period from the initial baseline measurement<br><br>Cardiovascular safety data was collected by looking at macrovascular events and episodes of congestive heart failure (CHF). The number of episodes of a common cardiovascular endpoint of cardiovascular mortality, non-fatal MI, or non-fatal stroke was 6 (2.2%) in glimepiride patients and 5 (1.9%) in ACTOS-treated patients. The number of hospitalizations due to CHF were equivalent in both arms. In the ACTOS-treated group, more patients were experienced a bone fracture than in glimepiride-treated group and in glimepiride there could be seen more patients with hypoglycemia and angina than in the ACTOS-treated group. | | |

## TCV-116 (1)

| Study title | CHARM (Candesartan in Heart failure Assessment of Reduction in Mortality) | | |
|---|---|---|---|
| **Outline** | This study was conducted to evaluate the clinical benefits of candesartan in patients with heart failure. | | |
| **Place** | Around 26 countries | **Total population** | 7,601 patients |
| **Status** | Data presented at the European Society of Cardiology (ESC) annual meeting in August 2003 demonstrated that candesartan could reduce both cardiovascular deaths as well as hospital admissions for heart failure, across a broad spectrum of patients with chronic heart failure. CHARM consists of following three studies.<br>**CHARM-Alternative**: (Candesartan vs. Placebo) Patients: LVEF *40% or lower, intolerance to ACE-I<br>In patients who were not taking ACE-inhibitors due to previous intolerance, candesartan significantly reduced the risk of cardiovascular death or hospital admissions for chronic heart failure, with an overall risk reduction of 23% (p<0.0004).<br>**CHARM-Added**: (Candesartan + conventional therapy vs. Conventional therapy) Patients: LVEF 40% or lower<br>In patients that were prescribed conventional therapy for chronic heart failure including an ACE inhibitor, candesartan demonstrated additional mortality and morbidity benefits. Candesartan significantly reduced the risk of cardiovascular death or hospital admissions for chronic heart failure by 15% (P=0.011) .<br>**CHARM-Preserved**: (Candesartan vs. Placebo) Patients: LVEF higher than 40%<br>The results showed that 11% risk reduction in favor of candesartan (P=0.118). There was also a significant 40% reduction in the number of patients diagnosed with new onset diabetes (47 vs. 77; P=0.005).<br>Pooled analysis of the three studies showed that candesartan provided a significant reduction in cardiovascular death (P=0.012) and also demonstrated a positive trend in the overall reduction in all cause mortality (P=0.055). Interestingly, it also demonstrated a significant 22% reduction in onset of new diabetes, with 163 new cases of diabetes on candesartan compared with 202 on placebo.<br>*LVEF: Left Ventricular Ejection Fraction. LVEF is a clinical indicator to evaluate degree of heart failure (Normal 60%-70%)<br>*Cardiovascular death: death of stroke, myocardial infarction | | |

## TCV-116 (2)

| Study title | DIRECT (DIabetic REtinopathy Candesartan Trial) | | |
|---|---|---|---|
| **Outline** | The world's first large scale clinical study to investigate prevention/treatment efficacy on diabetic retinopathy (candesartan vs. placebo) | | |
| **Place** | 30 countries | **Total population** | 5,231 patients |
| **Status** | Data from the DIRECT Programme, the first large-scale study programme assessing the effect of treatment with an angiotensin receptor blocker (ARB) on the incidence and progression of diabetic eye complications, was presented at the European Association of the Study of Diabetes (EASD) congress in Rome in September 2008. The data show a strong trend in favour of treatment with candesartan 32mg in reducing the incidence of diabetic retinopathy in Type 1 diabetes patients, although not statistically significant, and a significant increase in regression of diabetic retinopathy in Type 2 diabetes patients.<br>Study 1 'DIRECT-Prevent 1' (n=1,421) studied the effect of candesartan on the incidence of retinopathy (primary endpoint) in normotensive, normoalbuminuric Type 1 diabetes patients.<br>In Type 1 patients with no signs of diabetic retinopathy at baseline, candesartan caused an 18% reduction in the incidence of diabetic retinopathy as measured by 2-step change on the Early Treatment of Diabetic Retinopathy Study (ETDRS) scale (primary endpoint, p=0.0508), but a 35% reduction for 3-step change (post-hoc analysis, p=0.003).<br>Study 2 'DIRECT-Protect 1' (n=1,905) studied the effect of candesartan on the progression of retinopathy (primary endpoint) in normotensive, normoalbuminuric Type 1 diabetes patients already affected by retinopathy.<br>In the Type 1 diabetic patients with retinopathy at baseline there were no differences in the results in progression of retinopathy between the two treatment groups (p=0.85).<br>Study 3 'DIRECT-Protect 2' (n=1,905) studied the effect of candesartan on the progression of retinopathy (primary endpoint) in normoalbuminuric, normotensive or treated hypertensive, Type 2 diabetes patients with retinopathy.<br>Treatment with candesartan also reduced the risk of progression of retinopathy by 13% over placebo in Type 2 diabetes patients, primary endpoint, p=0.2. However, in these Type 2 diabetes patients with relatively early signs of diabetic retinopathy, candesartan increased the probability of regression of retinopathy by 34% compared with placebo (pre-defined secondary endpoint, p=0.009). | | |

## TCV-116 (3)

| Study title | CASE-J (Candesartan Antihypertensive Survival Evaluation in Japan) | | |
|---|---|---|---|
| **Outline** | Large scale clinical study of high-risk hypertensive patients in Japan | | |
| **Place** | Japan | **Total population** | 4,728 patients |
| **Status** | This is the first large-scale outcome study in Japan comparing BLOPRESS®, (generic name: candesartan cilexetil), angiotensin receptor blocker and amlodipine, a calcium antagonist, both of which are the most frequently prescribed medicines in Japan in each class. In the study, the incidences of cardiovascular (CV) events in 4,728 Japanese patients with high-risk hypertension were compared in the two treatment groups for 3 years or longer.<br>BLOPRESS reduced all-cause mortality by 15% compared with amlodipine, although this difference was not statistically significant. In obese patients with hypertension, in particular, BLOPRESS significantly reduced all-cause mortality by 49% compared to amlodipine (P=0.045). <Secondary endpoint><br>BLOPRESS significantly reduced new onset of diabetes by 36% compared to amlodipine (P=0.030). Stratified analysis revealed that this effect was conspicuous, particularly in obese patients with higher body mass index. | | |

## TCV-116 (4)

| Study title | HIJ-CREATE (The Heart Institute of Japan-Candesartan Randomized trial for Evaluation in Coronary Artery Disease) | | |
|---|---|---|---|
| **Outline** | Large-scaled outcome study with coronary artery disease patients with hypertension | | |
| **Place** | Japan | **Total population** | 2,049 patients |
| **Status** | During the American Heart Association's Scientific Session 2007, held at Orlando, Miami, the results of the HIJ-CREATE study ("CREATE study") were presented in late-breaking clinical trials session.<br>This is a large-scaled outcome study with coronary artery disease patients with hypertension in Japan, comparing the reduction of incidence of major adverse cardiovascular events ("MACE") between therapy with BLOPRESS and that with non-ARB standard therapy, and the total number of patients is 2,049.<br>・Reduction of incidence of MACE in patients with impaired renal function<br>BLOPRESS showed 21% reduction in incidence of MACE as compared to the non-ARB standard therapy. (P=0.039)<br>・The new onset rates of diabetes mellitus<br>The new onset rate with BLOPRESS and non-ARB standard therapy are 1.1% and 2.9% respectively. (P=0.027) | | |

## Research Activities

### ■ Main joint research activities

#### (1) Joint researches with domestic research organizations and companies

| Partner | Research subject | Schedule |
|---|---|---|
| Kirin Brewery Company Ltd.<br>(Now Kyowa Hakko Kirin Ltd.) | Licensing-in of the human antibody technology | 2003/7- |
| Kyoto University | Research collaboration for basic and clinical research project of discovering treatments for obesity and schizophrenia based on CNS control | 2011/1-2016/3 |
| Osaka University | Joint research on development of platform for practical application and commercialization of nano-particle vaccines | 2012/2-2015/1 |

#### (2) Joint research with overseas research organizations and companies

| Partner | Country | Research subject | Schedule |
|---|---|---|---|
| Oxford Centre for Diabetes, Endocrinology and Metabolism | UK | Partnership with Oxford Diabetes Centre | 2002/4-2013/10 |
| XOMA Ltd. | US | Joint research on discovery, development and production technologies of monoclonal antibody | 2006/11- |
| Alnylam Pharmaceuticals, Inc. | US | Collaboration for Discovery and Development of RNAi Therapeutics | 2008/5-2013/5 |
| Seattle Genetics | US | Research collaboration on Antibody-Drug Conjugate | 2009/3- |
| CellCentric | UK | Exclusive licensing of one of the CellCentric's epigenetics projects for the development and commercialization in oncology field | 2010/2- |
| BC Cancer Agency/Vancouver Prostate Centre | Canada | Research collaboration for discovery of novel candidate targets for cancer treatment | 2010/3-2013/3 |
| University College London | UK | Research collaboration on development of novel cancer treatment | 2010/3-2014/3 |
| Sage Bionetworks | US | Research collaboration on discovering effective therapeutic targets for Central Nervous System (CNS) disease | 2010/11-2015/6 |
| Florida Hospital, Sanford-Burnham Medical Research Institute | US | Research collaboration to target obesity | 2010/12-2015/2 |
| Zinfandel Pharmaceuticals | US | Licensing agreement for Alzheimer's Disease Biomarker TOMM40 for the risk of Alzheimer's disease | 2010/12- |
| Samyang Corporation | S. Korea | Joint research on novel DDS platform technology for RNAi therapeutics | 2011/4-2013/12 |
| Structural Genomics Consortium | Canada | Participation in consortium to advance basic research on selected drug targets based on three-dimensional structures of human proteins | 2011/7-2015/6<br>*Takeda joined 2012/4 |
| BC Cancer Agency | Canada | Research collaboration to explore new drug targets based on gene analysis | 2012/8-2015/7 |
| Advinus Therapeutics | India | Discovery collaboration focused on novel targets for major therapeutic areas, including Inflammation, CNS, and Metabolic diseases | 2012/10-2015/9 |
| Resolve Therapeutics | US | Collaboration to develop compounds for the treatment of Systemic Lupus Erythematosus (SLE) | 2013/2- |
| Tri-Institutional Therapeutics Discovery Institute | US | Collaboration of academic institutions and industry to more effectively develop innovative treatments and therapies | 2013/10 -2016/9 |
| Trianni, Inc. | US | Agreement for use of Trianni's next generation transgenic mouse platform for the generation of human monoclonal antibodies against disease targets in all therapeutic areas | 2014/3- |

# XI. News Releases

Major news releases during September 2013 - March 2014 are as below.

Please refer to our web site for details(http://www.takeda.com).

| Date | Summary |
|---|---|
| 2-Oct | Tri-Institutional Therapeutics Discovery Institute, Inc. Launched by Memorial Sloan-Kettering Cancer Center, The Rockefeller University and Weill Cornell Medical College, and Partnership Formed with Takeda Pioneering Collaboration with Research-Based Global Pharmaceutical Company to Conduct Early-Stage Drug Discovery |
| 7-Oct | Takeda Highlights Data from Clinical Trial of Investigational Norovirus Vaccine Candidate |
| 19-Nov | Oral Proteasome Inhibitor MLN9708 Enters into Phase 3 Clinical Study in Japan |
| 30-Nov | Takeda Appoints Chief Operating Officer |
| 4-Dec | Teva and Takeda Announce Agreement for Glatiramer Acetate for Multiple Sclerosis Treatment in Japan |
| 20-Dec | Takeda Announces Exclusive License and Option Agreement with Natrogen for Development of Natura-alpha for Inflammatory Bowel Disease |
| 25-Dec | Takeda Submits a New Drug Application for Fomepizole in Japan for the Treatment of Ethylene Glycol and Methanol Poisonings |
| 25-Dec | Takeda Announces Extension of FDA PDUFA Action Date for Vedolizumab for Ulcerative Colitis |
| 27-Dec | Takeda Announces Termination of Fasiglifam (TAK-875) Development |
| 8-Jan | Takeda's New Investigational Drug Vedolizumab Entered Phase 3 Clinical Trials in Japan for the Treatment of Ulcerative Colitis and Crohn's Disease |
| 14-Jan | Takeda Announces Varicella Vaccine Sales Agreement with the Research Foundation for Microbial Diseases of Osaka University in Japan |
| 17-Jan | Takeda Announces the New Drug Application Approval of ADCETRIS® (brentuximab vedotin) in Japan for the Treatment of Malignant Lymphoma |
| 22-Jan | Brintellix® (vortioxetine) for the treatment of major depressive disorder in adults is now available in U.S. pharmacies |
| 24-Feb | Takeda Announces a Re-alignment of its Marketing System in Japan |
| 28-Feb | Takeda Submits a New Drug Application for TAK-438 in Japan for the Treatment of Acid-related Diseases |
| 7-Mar | Takeda Announces the Appointment of Third-party Investigators Regarding Candesartan Antihypertensive Survival Evaluation in Japan (CASE-J) |
| 7-Mar | Takeda Submits a New Drug Application for Trelagliptin Succinate (SYR-472) in Japan for the Treatment of Type 2 Diabetes |
| 13-Mar | Takeda Announces New Global Operating Structure and Changes to Reporting Lines Under Chief Operating Officer from April 1st |
| 24-Mar | Takeda Announces the New Drug Application Approval of Zacras® Combination Tablets LD and Zacras® Combination Tablets HD in Japan for the Treatment of Hypertension |
| 24-Mar | Takeda Announces the New Drug Application Approval of TAKELDA® Combination Tablets, the Fixed Dose Combination of TAKEPRON® and Low-Dose Aspirin, in Japan |
| 24-Mar | Takeda Receives Positive CHMP Opinion for Entyvio® (vedolizumab) in Europe for the Treatment of Ulcerative Colitis and Crohn's Disease |
| 27-Mar | Otsuka and Takeda Announce a Co-promotion Agreement in Japan of TAK-438 For the Treatment of Acid-related Diseases in the Gastrointestinal Therapeutic Area |
| 28-Mar | Takeda Presents Additional Data from the EXAMINE Cardiovascular Safety Outcomes Trial at the American College of Cardiology's 63rd Annual Scientific Session |
| 31-Mar | Takeda Announces the New Drug Application Approval of Cell Cultured Influenza vaccine H5N1 "TAKEDA" 1mL and Cell Cultured Influenza vaccine (Prototype) "TAKEDA" 1mL in Japan for Prevention of Pandemic Influenza |
| 31-Mar | Transfer of Takeda Analytical Research Laboratories business to Sumika Chemical Analysis Services |
| 31-Mar | Takeda and Trianni Sign Licensing Agreement For Use of Trianni Transgenic Mouse Platform |
| 31-Mar | Dainippon Sumitomo Pharma and Takeda Announcethe European Marketing Authorization for Latuda® (lurasidone)- a New Atypical Antipsychotic Medication for Adults with Schizophrenia |

Takeda Pharmaceutical Company Limited