

Research & Development

Takeda pursues high-quality research and development through close collaboration between its R&D centers worldwide

In July 2009 Takeda started full-scale construction of its new research center situated astride the border between the two cities of Fujisawa and Kamakura in Kanagawa Prefecture. Aiming to complete construction in fiscal 2010, we will position the new research center as the linchpin of our global research network as we build research capabilities that will enable us to conduct world-class drug discovery research. In addition, we will improve teamwork between all divisions involved in R&D and reinforce measures to enable us to continually generate new drugs through our own R&D, as we strive to become a world-class pharmaceutical company.

Strengthening our Pipeline and Accelerating R&D Strategies Focused on Quality

Takeda has designated four core therapeutic areas within its operations: lifestyle-related diseases; oncology and urological diseases (including gynecological disorders); central nervous system diseases (including bone and joint disorders); and gastroenterological diseases. We are actively pursuing business in these fields based on our Tikarakobu Research Strategy, which is designed to enable focused deployment of research resources and the diversification of risk. The oncology field in particular is a key therapeutic area, second only to lifestyle-related diseases among our four core therapeutic areas. We formulated our R&D strategy for oncology around Millennium Pharmaceuticals, Inc., and we are pooling all the capabilities of our R&D centers worldwide to strengthen our pipeline for this field.

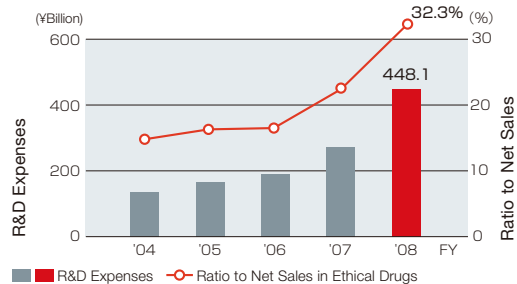
Thanks to progress in genome analysis and related areas, pharmaceutical research has benefited from a dramatic increase in the number of novel drug discovery targets. However, the probability of success at the clinical development stage has declined significantly at

almost all pharmaceutical manufacturers, reflecting the fact that they are now required to clearly differentiate their products from existing drugs and competitors' products in terms of efficacy and safety, while the safety requirements of regulating authorities in all countries have become more stringent. Industry-wide, the average R&D expenditure necessary to bring one product to market has increased more than 20-fold over the last 30 years, from US\$56 million to US\$1,246 million.* To survive in this environment, we are focusing current policy on high quality in our R&D more than ever before. Takeda must ensure right from the drug discovery stage that it is developing compounds that can fully address medical needs. In addition, we believe that it is crucial when deciding whether to proceed to Phase III clinical trials—the most expensive stage of the drug development process—to evaluate from the perspectives of both scientific evidence and profitability. Looking ahead, we will enact a range of measures based on closer collaboration between our R&D centers worldwide to improve the probability of success in new drug development.

* Source: Parexel's Bio/Pharmaceutical R&D Statistical Sourcebook

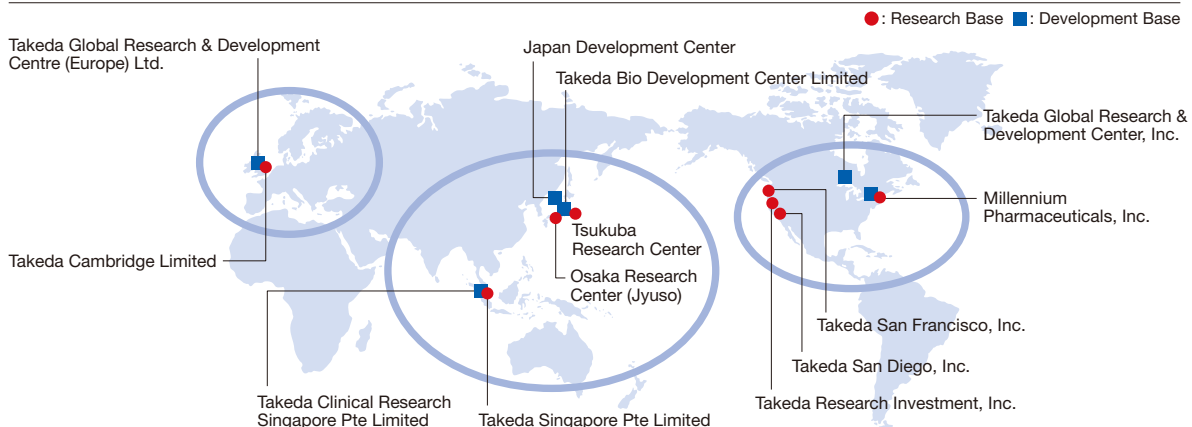


R&D Expenses / Ratio to Net Sales in the Ethical Drug Business



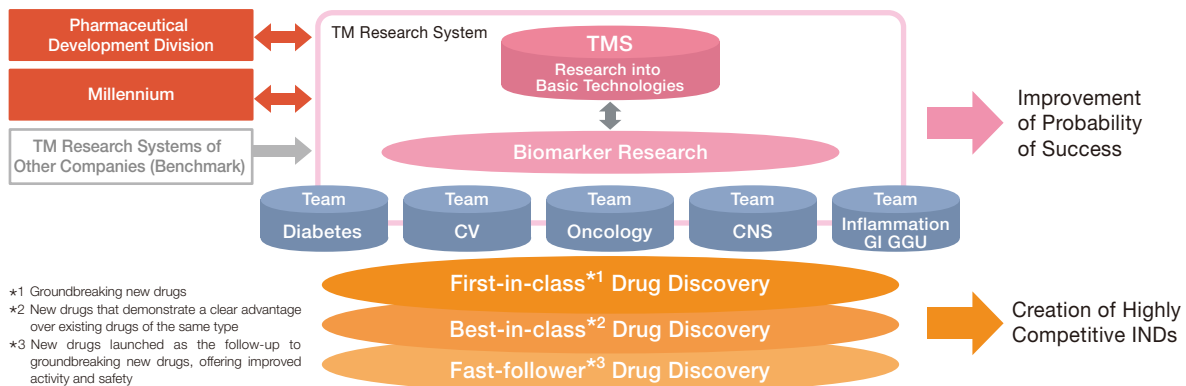
* Fiscal 2008 includes in-process R&D expenses associated with the integration of TAP Pharmaceutical Products Inc. and Millennium Pharmaceuticals, Inc.

Global Research and Development Bases



Takeda will actively adopt measures to ensure high-quality R&D and introduce new drug discovery technologies to enable ongoing new drug development derived from in-house R&D

Enhancement of Translational Medicine Research



Emphasis on Differentiation from the Early Stages of Research

In order to generate a reliable stream of high-quality drug discovery targets and develop competitive candidate compounds that will lead to marketable drugs, we intend to pursue measures that, right from the early stages of research, are more focused on such considerations as the product concept, positioning within the target market, novelty, and what sets the product apart from others. Where strategies guiding the overall direction of research are concerned, the Strategic Product Planning Department and development and marketing divisions in and outside Japan are collaborating to draw up strategies for research portfolios in each therapeutic field. They are also reviewing the order of priority assigned to each research theme in an appropriate and timely manner to enable optimal allocation of research resources. In the development stage we will propose and execute an optimal development plan for each compound created in the research stage, based on differentiation between first-in-class, best-in-class, and fast-follower. For compounds with new action mechanisms that are strong candidates to become first-in class, we will apply POC (Proof of Concept) at an early stage, and focus on marketable drugs only, since the development risk is very high. For compounds that are highly likely to become best-in-class, we will adopt differentiation-focused development strategies and planning.

Reinforcing Translational Medicine Research to Enable More Efficient R&D

Takeda is working to increase the probability of success in clinical development projects by reinforcing its Translational Medicine (TM) research to establish a framework that will facilitate efficient R&D.

Translational Medicine Sciences (TMS) has been launched

as a new department with functions that straddle both the research and development divisions. Built on the existing foundation of translational medicine research at Takeda, TMS acts as a smooth link between non-clinical and clinical trials, allowing findings from up-to-date basic research to be applied directly in clinical development for use in treating patients as well as tailoring of non-clinical programs keeping clinical end-users in mind. TMS uses various technologies such as employing the results of tests using cells and animals to develop new human biomarkers and evaluate new drug candidates, or mathematical modeling of pharmacological data to optimize the clinical trial design to help minimize future development risk and make it easier to determine the types of patients who will respond well to a drug. TMS is therefore expected to increase the probability of success in new drug development.

We intend to further reinforce TM research across the Takeda Group by facilitating an open information sharing environment between R&D and including TMS as an integral part of the project progression decision making process. At the same time, we will collaborate more closely with Millennium



(From left): Hiroyuki Odaka, General Manager, Pharmaceutical Research Div.
Dr. Nancy Joseph-Ridge, General Manager, Pharmaceutical Development Div.

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to make use of the expertise and technologies that company has amassed in the oncology field as part of our efforts to further enhance TM research in the Takeda Group.

Initiatives to Prepare for the Paradigm Shift in Drug Discovery and Reinforcement of CMC Research

Takeda is moving aggressively to conduct drug discovery based on new infrastructure technologies to prepare for a future paradigm shift. One such infrastructure technology is the development of antibody drugs, which use biotechnology to create antibodies that selectively inhibit the function of molecules according to their type. This technology has already established itself in the oncology field, and is likely to develop dramatically in future. Another infrastructure technology offering future market potential is nucleic acid drugs, which enable treatment at the genetic level, making it possible to identify drug discovery targets that offered little hope of success using other means such as low molecular or antibody drugs.

We stepped up the pace of our research in the antibody drugs field by establishing Takeda San Francisco, Inc. (TSF) in 2007, and we are working to establish in-house manufacturing capabilities to ensure reliable quality and low-cost production. Where nucleic acid drugs are concerned, up to now we have bolstered our research base by importing new technologies and conducting collaborative research. Going forward, we will work to achieve stabilization of the drugs inside the patient and targeting of the drugs to internal organs. We believe that further reinforcement of our CMC (Chemistry, Manufacturing and Control) research will be crucial in this regard. It will also be essential that CMC research functions operate in collaboration with our drug discovery research, and development departments. CMC research entails a comprehensive approach to supporting



One of the immune system's so-called "natural killer cells" attacks a cancer cell

pharmaceutical manufacturing and quality control. It includes devising pharmaceutical manufacturing methods and planning formulations, manufacturing and packaging, as well as determining analysis and assessment methods. When it was restructuring its global R&D network in April 2009, Takeda separated the CMC Research Center from the Pharmaceutical Production Division to enable it to function more effectively. At the R&D stage, the center maximizes the added value of our products by developing manufacturing processes for, and assessing the characteristics of drug substances, planning pharmaceutical formulations and manufacturing processes and assessing their functionality, and investigating the possibility of increasing scale for commercial production. Subsequently, at the commercialization stage, the center helps to ensure that we can supply pharmaceuticals reliably by introducing new technologies as appropriate at plants manufacturing products for market.

In addition to antibody drugs and nucleic acid drugs, another next-generation therapy Takeda is focusing on is regenerative medicine. We are pursuing research into regeneration of pancreatic and nerve cells, and other areas where we can leverage our strengths in low molecular drugs. Takeda is also involved in iPS cell-related projects. We are participating in the Project to Promote Application of iPS Cell Treatment, led by Professor Shinya Yamanaka at Kyoto University. We are also participating in the iPS Cell Project funded by Japan's New Energy and Industrial Technology Development Organization (NEDO) and have begun work to assist in efficiently identifying development candidates, reducing time required for drug discovery research and promoting the development of safer drugs.

Through efforts such as these, Takeda will strive to ensure that it continues to conduct competitive drug discovery.



(From left): Yoichi Okumura, General Manager, Intellectual Property Dept.
Tetsuo Miwa, General Manager, CMC Center