

Pharmaceuticals business sector



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Treating and curing

Merck improves quality of life with products such as Euthyrox® to treat thyroid disorders as well as treatments for hormone disorders using the patient-friendly electronic auto-injection device Easypod®.



Merck Serono



Merck Serono is the largest division of Merck. It focuses on specialist therapeutic areas and markets innovative prescription drugs of chemical and biotechnological origin, including monoclonal antibodies and other therapeutic proteins, in more than 150 countries.

Key therapeutic areas/products

- Oncology: Erbitux® (solid tumors)
- Neurodegenerative Diseases: Rebif® (multiple sclerosis)
- Autoimmune and Inflammatory Diseases: Raptiva® (psoriasis)
- Fertility: Gonal-f®, Pergoveris™, Luveris®, Ovitrelle®, Crinone®, Cetrotide® (infertility)
- Endocrinology: Saizen® (growth hormone disorders), Serostim® (HIV-associated wasting)
- CardioMetabolic Care: Glucophage® family (type 2 diabetes), Concor® family (cardiovascular diseases), Euthyrox® (thyroid disorders)

Key events in 2008

- Return on sales (ROS) rises from 8.0% to 11.9%
- Approvals of Erbitux® in the EU for first-line treatment of head and neck tumors and metastatic colorectal cancer (KRAS wild-type) and in Japan for the treatment of metastatic colorectal cancer after the failure of irinotecan
- Groundbreaking ceremony for the expansion of the production site in Corsier-sur-Vevey (Switzerland) to manufacture biological therapies
- Approval of Kuvan® in the EU for the treatment of hyperphenylalaninemia resulting from phenylketonuria or BH4 deficiency

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Achieving growth with new therapeutic options

In 2008, the Merck Serono division generated total revenues of € 4,987 million, 12% more than in 2007. The continuous growth in sales was primarily the result of the solid increases achieved by our main products, for example the biological drugs Rebif®, Erbitux® and Gonal-f® as well as classic products such as Concor® and Glucophage®. We achieved 58% of sales, equivalent to € 2,677 million, with biological drugs. Rebif® was once again our top-selling product. Global sales of this drug for the treatment of relapsing forms of multiple sclerosis (MS) rose to € 1,331 million in 2008 – an increase of 9.3% over the previous year.

Sales of the targeted cancer therapy Erbitux® continued to grow at a strong double-digit rate, increasing by 20% to € 565 million in 2008. Apart from the approval of Erbitux® in the European Union for first-line treatment of head and neck tumors and metastatic colorectal cancer (KRAS wild-type tumors), we also expanded our presence in the key market of Japan. The approval of Erbitux® in Japan gives physicians and patients a new therapeutic option in the second- and third-line treatment of metastatic colorectal cancer. In addition, we laid the cornerstone for the expansion of our biotech production in Corsier-sur-Vevey (Switzerland) in which we will invest a total of around € 300 million. By expanding this site, we will be able to produce greater quantities of biotherapeutics, for example the oncology drug Erbitux® as well as treatments for autoimmune and inflammatory diseases.

www.merckserono.com

We placed the cornerstone for the expansion of our biotechnology production in Corsier-sur-Vevey.

Operating result rises sharply

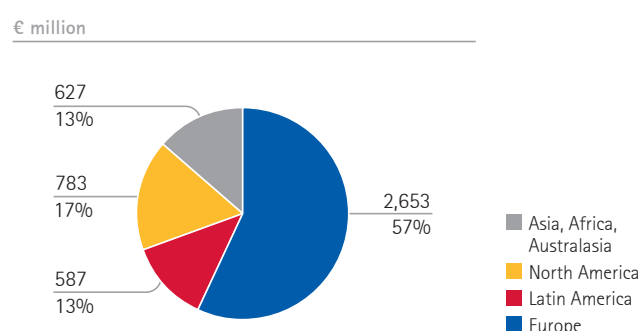
Gross margin increased by 11% to € 4,191 million over the previous year. The operating result rose by 66% to € 594 million. This increase was due, among other things, to the conclusion of restructuring and integration measures following the acquisition of the former Serono. In addition, we increased our royalty income by 25% to € 337 million in 2008.

In Europe, sales by the Merck Serono division grew by 8.7% to € 2,653 million. Our largest market was France, where sales increased by 7.7% to € 625 million. Sales in Germany rose only slightly by 1.7% to € 484 million mainly as a result of restrictive health policies. In both Italy and Spain, sales advanced by 10% and were virtually on a par at € 296 million and € 295 million, respectively. Smaller markets such as Turkey, Russia and the Czech Republic posted strong sales increases of 14%, 48% and 40%, respectively.

Merck Serono | Key figures

€ million	2008	2007	Δ in %
Total revenues	4,987	4,458	12
Gross margin	4,191	3,765	11
R&D	1,074	879	22
Operating result	594	357	66
Exceptional items	-354	-744	-52
Free cash flow (FCF)	554	-6,505	-
FCF before acquisitions and disposals	559	774	-28
ROS in %	11.9	8.0	

Merck Serono | Sales by region



The Merck Serono division has strengthened its position in the North American market.

We expanded our position in North America, where sales rose by 7.2% to € 783 million. In Latin America, we recorded a 19% increase in sales. In Brazil, our largest market, sales grew sharply by 33% to € 196 million. Sales in Venezuela and Colombia surged by 26% and 46%, respectively, whereas in Mexico, sales declined by 8.5% due to overstocking by wholesalers. Sales grew by 20% in the region Asia, Africa, Australasia, primarily thanks to the success in China, where sales jumped by 84% to € 114 million, and Japan, which posted a 64% rise in sales to € 30 million as well as good growth in smaller markets such as Saudi Arabia and Algeria.

Return on sales (ROS) amounted to 11.9% in 2008. Nominal free cash flow was € 554 million, considerably more than in 2007, the year in which we acquired Serono. By contrast, free cash flow adjusted for acquisitions and disposals declined by 28% to € 559 million with the termination of a program to sell receivables in Italy (details can be found on page 99).

Therapeutic areas

	Research	Development	Marketing
Oncology	■	■	■
Neurodegenerative Diseases	■	■	■
Autoimmune and Inflammatory Diseases	■	■	■
Fertility	■	■	■
Endocrinology		■	■
CardioMetabolic Care and other products			■

Oncology

Erbix[®] offers new prospects in the treatment of head, neck and lung cancer.

With the targeted oncology drug Erbix[®] (cetuximab), Merck Serono has not only considerably increased the number of treatment options available in colorectal cancer, but also opened up new medical prospects in the treatment of head and neck cancer as well as lung cancer. In 2008, our Oncology business unit generated sales of € 574 million. The majority share was attributable to Erbix[®], which achieved a 20% increase in sales to € 565 million. Erbix[®] currently holds marketing authorizations in 76 countries worldwide.

In July, the European Commission approved the expanded use of Erbix[®] in combination with chemotherapy to include not only second- and third-line treatment but also first-line treatment of patients with epidermal growth factor receptor (EGFR)-expressing, KRAS wild-type metastatic colorectal cancer. Patients with KRAS wild-type tumors, which occur in up to 65% of cases, are most likely to respond to Erbix[®], making this drug the first tailored therapy in first-line treatment of metastatic colorectal cancer. As expected, the sales growth rate of Erbix[®] slowed from the second to the third quarter of 2008. This was due to the fact that KRAS testing had to be implemented as a standard

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diagnostic procedure. Accordingly, the number of second- and third-line patients initially declined as a result of the focus on patients with KRAS wild-type tumors. In the course of expanded approval, we expect prescriptions for first-line treatment to increase, thereby more than compensating for the lower number of patients in second- and third-line treatment over the medium term. A crucial factor is that reimbursement in different countries is being granted at different points in time.

Further approvals of Erbitux®

In November, Erbitux® was approved in the European Union in combination with platinum-based chemotherapy for treatment of head and neck tumors. This approval is based primarily on the results of the EXTREME study, showing for the first time in 30 years a significant survival advantage in first-line treatment setting. In addition, we received marketing authorization in Japan for the use of Erbitux® in combination with irinotecan in metastatic colorectal cancer – giving pretreated patients access to this new treatment. Merck Serono, Bristol-Myers Squibb and ImClone Systems jointly market Erbitux® in Japan. Our marketing partners receive 50% of profits.

We are working to further expand the range of approved indications for Erbitux®. For example, we submitted an application to the European Medicines Agency (EMA) to approve Erbitux® for first-line treatment of epidermal growth factor receptor (EGFR)-expressing, advanced non-small cell lung cancer (NSCLC).

Neurodegenerative Diseases

Sales by this therapeutic area were almost exclusively attributable to Rebif® (interferon beta-1a). This product is the leading treatment for relapsing forms of multiple sclerosis (MS) outside the United States in terms of sales. Generating sales of € 1,331 million, or 9.3% more than in 2007, Rebif® was once again the top-selling product of the Merck Serono division. Adjusted for currency effects, sales growth amounted to 13%, mainly due to the weak U.S. dollar. We achieved around one-half of Rebif® sales in Europe. The new formulation, which offers improved injection tolerability, has meanwhile been introduced in all countries of the European Union. In 2008, the new formulation of Rebif® was approved in many countries around the world, including Australia, Argentina, Brazil and South Korea. Discussions with the U.S. Food and Drug Administration concerning approval are ongoing. Within the EU, the key markets of Italy and Spain showed exceptionally strong growth. More than one-third of sales were generated in North America, where sales increased by 10% to € 530 million over the previous year. In Latin America, sales remained at the previous year's level overall. However, in Brazil, a young market with considerable potential, we recorded strong double-digit growth. The highest growth rate (+20%) was achieved in Asia, Africa, Australasia, our smallest region.

Rebif® is the top-selling product of the Merck Serono division.

An established core therapy for multiple sclerosis

In 2008, we marked the tenth anniversary of Rebif®. Owing to its proven efficacy and favorable risk-benefit profile, Rebif® has become a core therapy for MS. It is now available in more than 80 countries. According to World Health Organization (WHO) estimates, up to 2.5 million people suffer from MS worldwide. The safety profile of Rebif® is supported by a robust, ongoing clinical development and treatment experience estimated at more than 600,000 patient-years to date.

Autoimmune and Inflammatory Diseases

Sales of our psoriasis treatment Raptiva® (efalizumab) rose by 22% to € 93 million. Raptiva® is approved in more than 60 countries around the world. Owing to sharply lower sales expectations, product technology assets were written off in full, leading to an expense of € 195 million. In the United States, Raptiva® is marketed by Genentech.

Raptiva® is approved for the treatment of adult patients with moderate to severe chronic plaque psoriasis. In some countries, this indication is further restricted to patients who have failed to respond to, or who have a contraindication to, or are intolerant to certain other systemic therapies. Since its approval, approximately 46,000 patients have been treated with Raptiva® worldwide.

However, since October 2008, Merck Serono has been notified of a reported side effect, namely a limited number of confirmed cases of progressive multifocal leukoencephalopathy (PML), a usually fatal viral infection of the central nervous system. The Merck Serono division and the regulatory agencies are reviewing the situation carefully and taking the necessary measures.

Fertility

The Merck Serono division is the global leader in developing and providing drugs to treat infertility. We are the only manufacturer of recombinant versions of all three main gonadotropin hormones. Sales by the Fertility therapeutic area increased 8.9% to € 565 million in 2008. Adjusted for the impact of currency, sales growth amounted to 13%. This was due to North America, where more than 20% of sales are generated. Growth was also above average in Asia, Africa, Australasia, some central European countries and Latin America.

Gonal-f® remains on a growth course

Gonal-f® (follitropin alfa for injection) maintained its position as the world's leading female fertility drug in 2008. This recombinant version of the follicle-stimulating hormone (FSH) is prescribed to supplement or to replace natural FSH. It has been approved in more than 100 countries. Sales rose by 5.9% to € 460 million. Growth slightly exceeded that of the gonadotropin market and was mainly attributable to strong double-digit growth rates in Latin America and Asia, Africa, Australasia, especially Brazil and China. We generated around one-half of Gonal-f® sales in Europe, where sales

Gonal-f® was the leading global female infertility treatment in 2008.

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were maintained at the previous year's level. In particular, sales grew more strongly in Italy and France than the average for the region. In North America, Gonal-f® gained additional market share. However, negative currency effects reduced the double-digit organic growth rate. In Japan, where Gonal-f® is approved to treat male infertility, we filed for regulatory approval in October to expand the indication to include female infertility.

Merck Serono is continually investing in the further development of its products and delivery devices. A new and improved version of the Gonal-f® pen has meanwhile been approved in more than 70 countries. Our efforts to launch the product globally continue.

Two hormones in a single injection

Pergoveris™ is our new drug for the stimulation of follicular development in women with severe luteinizing hormone (LH) and follicle stimulating hormone (FSH) deficiency. It is the first biotech drug based on the combination of both substances in a single subcutaneous injection. Pergoveris™ got off to a successful start, posting sales of € 14 million in the first year since its approval in the member states of the EU as well as Iceland, Liechtenstein and Norway.

Pergoveris™ is our new, additional drug for the stimulation of follicular development.

Ovidrel®/Ovitrelle® (choriogonadotropin alfa), a recombinant version of the natural pregnancy hormone hCG, is used to trigger ovulation in women who are undergoing assisted reproduction techniques. It is the first and only recombinant hCG offered in a ready-to-inject, prefilled syringe that is easy to use. The product generated sales of € 34 million, or 21% more than in 2007. This was due mainly to strong growth in Europe.

Endocrinology

With the specialized therapies and innovative drug delivery devices offered by its Endocrinology therapeutic area, the Merck Serono division is pursuing a clear aim: to improve the lives of patients affected by endocrine and metabolic disorders. Sales in this therapeutic area increased by 4.8% to € 229 million over the previous year. The top-selling product is Saizen®, a recombinant human growth hormone, which generated sales of € 172 million. Demand for Saizen® remained strong, especially in Europe, where sales grew 9.3%. The drug is marketed in most countries for the treatment of growth hormone deficiency in children and adults, as well as in children born small for gestational age (SGA), with Turner syndrome or chronic renal failure. According to expert estimates, the prevalence of growth hormone deficiency in children is between 1 in 4,000 and 1 in 10,000. Yet adults are also affected. In the United States alone, more than 50,000 people suffer from growth hormone deficiency and every year, 6,000 new cases are reported. In the United States, the Endocrinology therapeutic area also offers Serostim®. It is used to treat patients suffering from HIV-associated wasting, which is estimated to affect up to 8% of HIV-infected individuals.

Easypod® electronic auto-injection device drives sales growth of Saizen®

The good development of Saizen® was favorably impacted by the increasing use of the electronic auto-injection device Easypod®. This first delivery device of its kind has made once-daily administration easier for patients and medical professionals. In particular, it helps to monitor compliance. Since the launches in Europe, Australia, Latin America, North America and selected Asian markets, the uptake of Easypod® has increased among patients with growth hormone deficiency.

Kuvan® approved in Europe for the treatment of hyperphenylalaninemia

In the fourth quarter of 2008, the European Commission granted marketing authorization for Kuvan® for the treatment of hyperphenylalaninemia (HPA) due to phenylketonuria (PKU) or tetrahydrobiopterin (BH4) deficiency. HPA is an abnormally high concentration of phenylalanine in the blood, which can cause serious brain damage in infants and children, and transient to lasting neurocognitive impairment in adult patients if a strict diet is not adhered to at all times. Kuvan® is the first drug approved in Europe to treat this rare disease.

We are developing Kuvan® in partnership with BioMarin Pharmaceutical of the United States. Kuvan® was previously granted orphan drug designation by both the FDA and the EMEA. Consequently, Kuvan® has market exclusivity in this indication for ten years in the European Union and for seven years in the United States.

CardioMetabolic Care and other products

The interrelationships between diabetes, cardiovascular diseases and thyroid disorders are the causes of many complex clinical pictures.

More and more physicians are adopting an integrated approach to treat diabetes, cardiovascular diseases and thyroid disorders as they meanwhile attribute the causes of many complex clinical pictures to the multifaceted interrelationships between these conditions. In order to offer physicians and patients effective therapeutic approaches, the Merck Serono division has combined its portfolio of drugs to treat patients with these diseases in its CardioMetabolic Care therapeutic area. Sales by the CardioMetabolic Care therapeutic area increased by 11% to € 916 million, thanks to the strong growth of the Concor® franchise as well to solid growth of the Glucophage® and thyroid product franchises. Sales of other products, some of which we distribute only in individual markets, totaled € 921 million in 2008.

Bisoprolol – the leading beta-blocker in Europe

The Concor® franchise remains the top-selling group within CardioMetabolic Care. Sales of this beta-blocker containing the active ingredient bisoprolol increased by 14% to € 433 million in 2008. As the active ingredient in products such as Lodoz® and Concor®COR, bisoprolol is the leading beta-blocker in Europe. This region accounted for 73% of global sales. The growth of the Concor® family is due primarily to the excellent development of Concor®COR, sales of which increased 17%.

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Metformin recommended for type 2 diabetes

The active ingredient metformin remains the drug of choice for first-line therapy of type 2 diabetes. More than six million patients worldwide are benefiting from one of our oral diabetes therapies based on metformin. According to the International Diabetes Federation (IDF), around 246 million people have diabetes worldwide. Type 2 accounts for 85 to 90% of these cases, and the number continues to grow. According to a study by the Health Services Research Network, the number of type 2 diabetes cases in the United States alone is expected to increase to 29 million by 2050. The guidelines of the IDF, the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD) therefore recommend that newly diagnosed patients with type 2 diabetes be treated immediately with metformin, for example Glucophage®.

Despite generic competition, sales of the metformin franchise rose 9.0% to € 290 million. Branded products from the Glucophage® family generated a respectable 6.1% increase in sales to € 252 million. Glucophage XR® – a once-daily formulation – performed especially well, with sales surging by more than 33%.

Metformin is the drug of choice in type 2 diabetes.

Thyroid hormone Euthyrox® continues to deliver

Sales of our products to treat thyroid disorders increased by 10% to € 150 million in 2008. Nearly two-thirds of sales were attributable to Europe. Sales of the thyroid hormone Euthyrox® increased by 12% to € 129 million. Currently, around 12 million people in more than 70 countries take Euthyrox® every day.

With drugs to treat hypo- and hyperthyroidism as well as to prevent iodine deficiency diseases, Merck Serono is the second largest supplier worldwide. In Europe, Latin America and China we are number one. Thyroid disorders are one of the world's most prevalent diseases. According to epidemiological data, more than 300 million people suffer from hypothyroidism, i.e. underactivity of the thyroid gland, while not even 20% of them are currently being treated. We are therefore working to educate the public and improve awareness of the need to adequately manage this disease.

Globally, more than 300 million people suffer from hypothyroidism.

Research and development

Research and development spending increased markedly by 22% to € 1,074 million in 2008. This is equivalent to 22% of the division's total revenues. Apart from oncology we are focusing our research activities on innovative specialist therapies to treat neurodegenerative diseases such as multiple sclerosis as well as autoimmune and inflammatory diseases. Here and in the therapeutic areas of Endocrinology and Fertility we are simultaneously working on numerous development projects, for example, therapies to help infertile couples to conceive a child as well as treatments for growth disorders.

Overall, around 2,300 employees are engaged in the discovery and development of new drugs – mainly in Darmstadt, Geneva and Boston. They are working in highly specialized fields at the interface of innovative biotechnology and established pharmaceutical science. We improved our efficiency, starting seven new development projects in 2008. In addition, we submitted three of our innovative compounds for approval. We received four new marketing authorizations. In order to streamline our research and development activities, we terminated ten projects at the pre-clinical or clinical stage in 2008. As a result, our R&D pipeline consisted of 12 Phase I projects, eight Phase II projects and 11 Phase III projects in 2008.

We plan to strengthen our biotech R&D activities in the U.S.

With the announced expansion of our U.S. research site in Billerica, Massachusetts in a planned \$ 50 million investment, we will strengthen our biotech research and development activities in the United States. At the research center, which is scheduled to be completed by 2010, around 200 scientists, as well as 50 employees specializing in process development and protein production, will jointly discover and bring forward new treatments for unmet medical needs. The close proximity of protein production to research is expected to drive the rapid transition from research to manufacturing.

Scientific networks helping to secure the future

Cooperating in networks is of paramount importance to our success. In Germany, we belong to a top biotech cluster in the Rhine-Neckar region that is supported by the German federal government. Our researchers are participating in five subprojects. We are involved in pioneering work on new therapeutic strategies to eliminate tumor stem cells in collaboration with the German Cancer Research Center in Heidelberg.

We are cooperating with universities and have set up a fund for research projects.

Another example of our networks is the research alliance between the Merck Serono division and École Polytechnique Fédérale de Lausanne (EPFL). Our joint efforts are focused on the areas of neuroscience, oncology and drug delivery. The agreement has provided for three Merck Serono-endowed chairs as well as a major research fund. One of the projects is exploring the use of nanotechnology to achieve better drug uptake.

By restructuring our partnership with ZymoGenetics, we now have exclusive worldwide development and commercialization rights for atacicept as well as access to other innovative approaches. Merck Serono is developing the recombinant fusion protein atacicept as a potential therapy for autoimmune diseases such as lupus, rheumatoid arthritis and multiple sclerosis.

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Status of our innovative compounds (Status: December 31, 2008)

Therapeutic area	Compound	Indication	Status
Oncology	Erbix® (cetuximab) ¹	NSCLC	Filed
		Adjuvant colorectal cancer	Phase III
		Gastric cancer	Phase III
	Stimuvax® ²	NSCLC	Phase III
	Cilengitide	Glioblastoma	Phase III
	Erbix® (cetuximab) ¹	Breast cancer	Phase II
	Cilengitide	SCCHN	Phase II
	Tucotuzumab celmoleukin (EMD 273066/huKS-IL2)	SCLC	Phase II
	EMD 273063 (hu14.18-IL2)	Pediatric neuroblastoma and melanoma	Phase II
	Adecatumumab (MT201) ³	Solid tumors	Phase I
	Aurorakinase inhibitor (AS703569) ⁴	Solid tumors and hematological malignancies	Phase I
	NHS-IL2-LT (EMD 521873)	Solid tumors	Phase I
	DI17E6 (EMD 525797)	Solid tumors	Phase I
	Eg 5 inhibitor (EMD 534085)	Solid tumors und hematological malignancies	Phase I
	Survivac (cancer vaccine)	Solid tumors	Phase I
	MEK inhibitor (AS703026) ⁵	Solid tumors	Phase I
IMO-2055 ⁶ (TLR9 immunomodulator)	Solid tumors	Phase I	
Sonepcizumab (ASONEP™) ⁷	Solid tumors	Phase I	
Neurodegenerative Diseases	New formulation of Rebif®	Relapsing forms of multiple sclerosis (MS) EMEA: approved; FDA: filed	Approved/ filed
		Clinically isolated syndrome	Phase III
	Cladribine tablets	Relapsing forms of MS	Phase III
		Clinically isolated syndrome	Phase III
	Safinamide ⁸	Early-stage Parkinson's disease	Phase III
		Mid- to late-stage Parkinson's disease	Phase III
Atacicept ⁹	Multiple sclerosis	Phase II	
Autoimmune & Inflammatory Diseases	Atacicept ⁹	Systemic lupus erythematosus	Phase III
		Rheumatoid arthritis	Phase II
	Fibroblast growth factor 18 ⁹	Osteoarthritis	Phase I
Fertility	Hyperglycosylated FSH	Infertility (OI/ART)	Phase II
Endocrinology	Tesmarolin ¹⁰	HIV patients with lipodystrophy (only U.S.)	Phase III
	ARX 201 ¹¹	Growth hormone deficiency	Phase I

¹ Developed in cooperation with mit ImClone: Erbix® is a trademark of ImClone Systems, a wholly owned subsidiary of Eli Lilly & Co.

² Exclusive worldwide licensing rights acquired from Oncocyte Inc.

³ Collaboration with Micromet AG

⁴ Collaboration with Rigel Pharmaceuticals Inc.

⁵ All rights acquired from Santhera Pharmaceuticals AG

⁶ Inlicensed from Idera Pharmaceuticals Inc.

⁷ Collaboration with LPath, Inc. ASONEP is a trademark of LPath, Inc.

⁸ Collaboration with Newron Pharmaceuticals S.p.A.

⁹ Collaboration with ZymoGenetics Inc.

¹⁰ Collaboration with Theratechnologies

¹¹ Collaboration with Ambrx, Inc.

SCCHN: Squamous cell carcinoma of the head and neck

NSCLC: Non-small cell lung cancer

SCLC: Small cell lung cancer

OI/ART: Ovulation induction/Assisted reproductive technology

HARS: HIV-associated adipose redistribution syndrome

Personalized medicine:
A genetic test identifies
patients who will respond
best to treatment.

New therapeutic options for cancer treatment with Erbitux®

The results of numerous studies involving the monoclonal antibody Erbitux® (cetuximab) impressively demonstrate the consistent efficacy and versatility of this targeted cancer therapy. In metastatic colorectal cancer, for example, it is now possible to use the KRAS gene as a biomarker to identify those patients who are most likely to respond to treatment with Erbitux®, namely those with KRAS wild-type tumors.

The results of the Phase III CRYSTAL trial underline the value of Erbitux® as a new standard in first-line treatment of metastatic colorectal cancer. In this large randomized trial, 60% of all patients with KRAS wild-type tumors experienced significant tumor shrinkage when treated with Erbitux® in combination with chemotherapy – clearly exceeding the results achieved with chemotherapy alone. The ability of Erbitux® to shrink the tumor translated into a substantially decreased risk of tumor progression and a trend towards prolonged survival for all patients with KRAS wild-type tumors. Furthermore, effective tumor shrinkage might allow complete surgical resection of liver metastases, thereby enhancing the chance of a potential cure. A further randomized Phase II study (CELIM) investigated the efficacy of Erbitux® in combination with standard chemotherapy in patients with initially inoperable liver metastases. Tumor shrinkage was experienced by 79% of patients with KRAS wild-type tumors, and 43% of these patients underwent surgery. A complete surgical removal of the tumor was achieved in 34% – a chance for these patients to be cured. These data are among the best ever achieved for complete surgical removal of liver metastases in metastatic colorectal cancer.

Erbitux® in lung and gastric cancer

A Phase III clinical trial (FLEX) proved that in first-line treatment in combination with a platinum-based chemotherapy, Erbitux® can significantly prolong median overall survival of patients with non-small-cell lung cancer (NSCLC) across all histological patient subgroups. This effect was more pronounced in FLEX patients treated with Erbitux® who developed early acne-like rash, resulting in median overall survival of 15 months. Lung cancer is one of the leading causes of cancer death worldwide: Among men, it claims more lives – around 975,000 per year – than any other form of cancer. Among women, it is responsible for 376,000 deaths each year, second to breast cancer.

A further Phase III clinical trial (EXPAND) was started in the third quarter of 2008 to investigate the efficacy of Erbitux® in combination with chemotherapy as a new option in first-line treatment of gastric cancer. Every year, nearly 930,000 people are diagnosed with gastric cancer and around 700,000 die from it.

Expanding treatment possibilities in oncology

Two further compounds, Stimuvax® and cilengitide, are currently in Phase III development. Stimuvax® (BLP25 liposome vaccine) is an investigational therapeutic cancer vaccine designed to induce an immune response to cancer cells that express MUC1, a protein antigen over-expressed in many common cancers including lung, breast and colorectal cancer. Stimuvax® is currently in a Phase III study involving patients with non-small cell lung cancer (NSCLC). It is the first cancer vaccine in unresectable locally advanced NSCLC to enter Phase III clinical trial testing (START). The results of a randomized Phase II study found that after three years, almost twice as many patients with unresectable advanced NSCLC receiving Stimuvax® were still alive compared to patients in the control group.

Cancer vaccine Stimuvax®
designed to induce an immune
response to cancer cells.

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Merck Serono is currently evaluating the investigational integrin inhibitor cilengitide in glioblastoma – the most aggressive form of brain tumor – and in head and neck cancer. Cilengitide is thought to suppress the new formation of blood vessels (angiogenesis) and cut off the tumor from the blood supply. In addition, it is believed to target tumor cells directly. Following Phase II data, cilengitide is now being studied in a global Phase III trial (CENTRIC) to evaluate its efficacy in patients with newly diagnosed glioblastoma. All patients enrolled in the study are carriers of a specific chemical modification in a certain section of their DNA (methylated MGMT promoter). A further Phase II trial (ADVANTAGE) is evaluating the novel combination of cilengitide and Erbitux® in squamous cell carcinoma of the head and neck. In addition, we entered into a worldwide alliance with Lpath, Inc. of the United States to develop and commercialize sonopilizumab (ASONEP™), a Phase I monoclonal antibody currently being evaluated for the treatment of various cancer types.

Progress with the further development of Rebif®

Our development projects in Neurodegenerative Diseases are focused on innovative therapeutic options for multiple sclerosis (MS) and Parkinson's disease – two areas with high unmet medical needs. The Merck Serono division wants to expand the range of approved indications for the successful MS treatment Rebif® based on the outcome of clinical trials. One of the aims is to enable more patients in the early stages of the disease to benefit from treatment with Rebif®. In September, we completed the enrollment of more than 500 patients for the REFLEX trial, one of the most important studies on the further development of Rebif®. This 24-month Phase III registration study will examine the efficacy of the new formulation of Rebif® in clinically isolated syndrome. In this new indication, the study participants have so far only experienced MS-like attacks, but have not yet been diagnosed with clinically defined MS. The aim of the study is to investigate the therapeutic value of Rebif® prior to the outbreak of MS in these patients.

Initial results of the ongoing Phase IIb IMPROVE study after 16 weeks of treatment show that the primary endpoint has been met, confirming the therapeutic effect of the new formulation of Rebif® in MS patients. The number of active lesions in the brain as measured by magnetic resonance imaging was significantly lower than in patients treated with the new formulation of Rebif® compared with those receiving placebo in the control group.

Oral MS treatment – a new therapeutic option in development

With cladribine tablets, Merck Serono is developing a drug that – once approved – would represent the first therapeutic option for oral treatment of relapsing MS. Patients would only need to take this proprietary oral formulation of a nucleoside analogue a few times a year for a period of four to five days in a single daily dose, making treatment considerably more comfortable and improving the prospects for compliance. The U.S. Food and Drug Administration has given cladribine tablets fast-track designation. The safety and efficacy of cladribine tablets as an MS monotherapy in two dosage strengths were tested in a two-year Phase III registration study called CLARITY. This study, which involved more than 1,300 patients, was completed at the end of 2008. According to the results of the trial, which met the primary endpoint, the relapse rate was significantly reduced. Patients who received a lower total dose experienced a 58% relative reduction in annualized relapse rates versus placebo while patients

Studies are investigating whether Rebif® can be used in early-stage disease.

Cladribine tablets have fast-track designation from the FDA.

who received a higher total dose experienced a 55% reduction. We initiated ORACLE-MS, a further Phase III trial, at the end of September. It will evaluate the efficacy of cladribine in preventing conversion to definite multiple sclerosis in patients at risk of developing multiple sclerosis. The Phase II study ONWARD, which is currently underway, is examining the safety and efficacy of cladribine as an add-on to treatment to interferon beta, for example the new formulation of Rebif®.

Merck Serono is also developing atacicept for the treatment of multiple sclerosis. In April 2008, we initiated a Phase II study to evaluate the efficacy of atacicept in reducing central nervous system inflammation in patients with relapsing MS. In June, an exploratory Phase II trial was started to evaluate the efficacy of atacicept in optic neuritis. Inflammation of the optic nerve is a condition often experienced as an early clinical manifestation by patients with multiple sclerosis.

Safinamide – a potential add-on treatment in Parkinson's disease

Safinamide, an orally administered add-on treatment with a novel mechanism of action, is also in late-stage clinical trials. Together with the Italian pharmaceutical company Newron, we are developing safinamide for Parkinson's disease. A Phase III study to evaluate safinamide as an add-on treatment to levodopa in patients with advanced Parkinson's met its primary endpoint. The motor functioning of patients with advanced Parkinson's disease improved significantly. The "ON" times during which motor function reaches its highest levels were extended by 1.3 hours. In a Phase III study called MOTION, we are evaluating safinamide as an add-on therapy to dopamine agonist in early-stage disease.

Long-acting fertility hormone under development

Our research and development work in the therapeutic area of Fertility is aimed at helping infertile couples to conceive a child, delivering products for every phase of the reproductive cycle from ovulation to early pregnancy. With our innovative treatments and technologies, we want to help couples increase their chances of a successful pregnancy. In addition, it is our aim to continue making our products as patient-friendly as possible.

For example, we are developing a long-acting recombinant follicle-stimulating hormone (hyperglycosylated FSH), which would mean fewer injections for patients. We successfully completed the Phase II program in assisted reproduction (ART) and are ready to advance the compound to Phase III. Phase II studies to evaluate efficacy in inducing ovulation are still underway.

We terminated the development of anastrozole, an aromatase inhibitor for ovulation induction, in July 2008. Although Phase II dose finding studies were successfully completed, the substance did not show a promising profile to be advanced to Phase III when compared to clomiphene citrate, the standard treatment.

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New studies in systemic lupus erythematosus and rheumatoid arthritis

Our research and development activities in the Autoimmune and Inflammatory Diseases therapeutic area focus on proteins that modulate important mechanisms in the development of disease. The Merck Serono division is developing atacicept, a soluble fusion protein, for several indications including rheumatoid arthritis (RA). We completed patient enrollment in our two largest Phase II studies in RA and started another Phase II study in 2008. Data for the first two studies are expected in the second half of 2009.

Systemic lupus erythematosus (SLE), a chronic inflammatory disease where the immune system attacks the body's own tissues, is an area of high unmet medical need that primarily affects women. A Phase II/III study with atacicept in patients with SLE began in June. We discontinued one study of atacicept in lupus nephritis (LN), a particularly severe form of SLE affecting the kidneys, which was part of the ongoing SLE development program. This Phase II/III study combined atacicept with other medications (mycophenolate mofetil and corticosteroids) and was discontinued because of the occurrence of severe infections. These were thought to be the result of the underlying significant disease activity coupled with the concomitant use of several immunosuppressive medications. We are currently analyzing the data and redesigning the development plan for atacicept in lupus nephritis.

Thanks to its novel mechanism of action, fibroblast growth factor 18 (FGF 18) could be the first treatment for osteoarthritis that stimulates the repair of articular cartilage instead of simply treating the symptoms of this degenerative joint disease. A second Phase I trial in osteoarthritis was initiated at the end of 2008. In July, Merck Serono returned to the Swiss biotech company NovImmune the rights to develop and commercialize the human monoclonal antibody anti-CD 3 (NI-0401).

Development projects on growth disorders and metabolic diseases

Our researchers are working on a number of development projects on selected growth disorders and metabolic diseases in the therapeutic area of Endocrinology. The Merck Serono division can build on its long-standing experience in these therapeutic indications.

Our U.S. subsidiary EMD Serono acquired the commercialization rights to tesamorelin, a growth hormone-releasing factor analogue with therapeutic potential in a variety of anabolic and lipolytic indications. The compound is in the final stages of its second Phase III clinical trial to assess the safety and efficacy when used to reduce excess abdominal fat in HIV patients with lipodystrophy. The development of a high-dose recombinant human growth hormone for the treatment of HIV-associated adipose redistribution syndrome (HARS) was discontinued and an impairment loss was recognized for the intangible assets capitalized to date.

In cooperation with the U.S. biopharmaceutical company Ambrx, we are studying the long-acting growth hormone ARX-201 for the treatment of growth hormone deficiency.

In other projects we are working on the constant further development of our application devices.

Focus on proteins that modulate important mechanisms in the development of disease.

Consumer Health Care



The Consumer Health Care division offers consumers high-quality over-the-counter products for preventive health care and self-treatment of minor ailments.

Key products

- Mobility: Products to strengthen the joints, including the brands Seven Seas®, Seven Seas® JointCare and Kytta®
- Everyday Health Protection: Vitamins and minerals sold under brand names such as Cebion® and Diabion®; probiotic multivitamin products Bion®3 and Multibionta®
- Women's and Children's Health: Femibion®, a multivitamin product with folic acid and Metafolin® for pregnant and nursing women; Kidabion® (Haliborange®), a vitamin product for children
- Cough and Cold: Cold remedy Nasivin® (Iliadin®); flu remedy Sedalmerck®

Key events in 2008

- Double-digit organic growth of 12% in total revenues clearly exceeds market growth
- Acquisition of the Belgian company Bio-Fyt
- Divestment of the biManán® brand of diet products in Spain
- Strategic brands further strengthened
- Successful advertising campaign for Kytta® ointment with strong growth in Germany
- Expansion of business in the growth markets of China and India

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Growth with brands that consumers trust

Focusing on four health themes

Our Consumer Health Care division is a specialized supplier of over-the-counter products focused on four health themes: Cough and Cold, Mobility, Everyday Health Protection and Women's and Children's Health. Our main distribution channels are pharmacies, as well as retail chains and mail order in some countries. We are building on the strength of our well-known brands and the trust consumers place in them with respect to their quality and efficacy.

Total revenues of the Consumer Health Care division rose by 5.2% to € 442 million in 2008. Organically, we posted a double-digit sales increase of 12%, more than twice that of the estimated global OTC market. We are continuing to pursue a two-pronged strategy. On the one hand, we are increasingly focusing our business on our strategic brands, while on the other hand we are driving expansion in growth markets such as those of eastern Europe, Asia and Latin America.

In 2008, we continued to invest significantly to further develop our strategic brands. These were financed partly by the proceeds from the sale of the Spanish diet product brand biManán® to the French company Nutrition & Santé for € 11 million. While biManán® was the division's most important brand in Spain, it was only of local significance, did not focus on our health themes and recorded stagnant sales.

Strong currency impact in key markets

In many markets, negative currency effects seriously undermined our strong organic growth. The most significant impact was felt in the United Kingdom, a key market, as well as in the traditionally important markets of Mexico and Venezuela. By contrast, positive currency effects were registered in the growth markets of eastern Europe, for example Poland, the Czech Republic and Slovakia, though these were insufficient to offset the general trend.

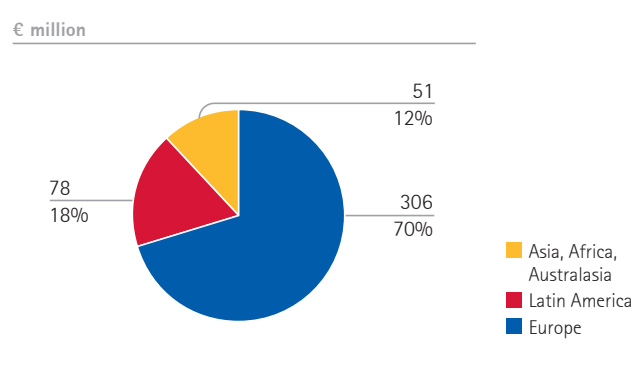
The operating result of the Consumer Health Care division increased to € 61 million, 2.9% more than in 2007. Free cash flow adjusted for acquisitions and disposals decreased by 19% to € 38 million mainly as a result of higher capital spending.

[www.merck.de/
consumerhealthcare](http://www.merck.de/consumerhealthcare)

Consumer Health Care | Key figures

€ million	2008	2007	Δ in %
Total revenues	442	420	5.2
Gross margin	294	284	3.5
R&D	17	12	40
Operating result	61	60	2.9
Exceptional items	-	-	-
Free cash flow (FCF)	5.6	47	-88
FCF before acquisitions and disposals	38	47	-19
ROS in %	13.9	14.2	-

Consumer Health Care | Sales by region



France is the largest market for our Consumer Health Care division.

Good performance in France

Europe remained our most important market. Sales totaled € 306 million. We performed well in the most important core markets, in many cases counteracting weak market developments. In France, where the market for over-the-counter prescription-free medicines declined by 3.2% in 2008, we increased sales by 4.2% to € 94 million in the same period. France was thus once again our largest market. Our subsidiary Merck Médication Familiale saw continued success there with the probiotic multivitamin brand Bion®, achieving a 21% increase in sales to € 23 million. Bion® is now the fifth-leading brand in the French OTC market. The strategic brand Femibion® for pregnant women and nursing mothers also posted a strong 12% increase in sales. Higher sales of strategic brands more than offset the decline in sales of cosmeceuticals from the local dermatology line, which fell to € 26 million. The success of our approach of focusing the business more strongly on strategic brands is apparent here. Merck Médication Familiale now ranks second in both the dietary supplement and OTC markets of France.

Portfolio streamlined in the United Kingdom

Sales in the United Kingdom declined by 16% to € 64 million, primarily as a result of the weakness of the British pound, which had a double-digit currency impact. As a consequence, sales by Seven Seas, our UK subsidiary, decreased by 12%. In local currency, however, sales increased by 2.6%. Seven Seas thus achieved its goal of stabilizing the business despite a 4% decline in the vitamins and supplements market. Compensation payments of around € 4 million from a supplier whose product impurities triggered a recall in 2006 had a positive effect.

At the end of September, we also sold the Petcare business for a low seven-digit figure, thus moving ahead with our plan to streamline the portfolio and divest non-core assets. Sales by Lamberts Healthcare, our mail order business with high-quality vitamins and minerals, stagnated in local currency terms in a weak market.

Kytta® gains market share in Germany

Sales in Germany increased by 16% to € 46 million in a market that declined by 2.5%. The largest contribution to sales came from the plant-based ointment Kytta® for muscle and joint pain. Following a successful advertising campaign, sales increased by 77% to € 14 million in 2008. As a result, Kytta® considerably increased its market share in Germany. Sales of the metafolin product Femibion® also developed favorably, increasing 14% to € 15 million.

Acquisition in Belgium

We increased sales in Belgium by 18% to € 18 million. In particular, we achieved strong sales gains with the strategic brands sold in Belgium under the Omnibionta® umbrella: Sales of Femibion® and Bion®3 increased by 43% and 24% respectively. Sales of the cold remedy Nasivin® grew by 6.7%. In December, we acquired the company Bio-Fyt for € 30 million in order to strengthen our market position and to expand the product portfolio. Bio-Fyt develops, markets and sells mobility, women's health and everyday health-protection products. The acquisition of Bio-Fyt is therefore in line with our strategy of focusing on specific health themes and achieving leading positions within these defined segments.

The acquisition of the Belgian company Bio-Fyt will expand the portfolio .

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Expanding business in eastern Europe

Business in the growth markets of eastern Europe developed dynamically. In Poland, sales totaled € 26 million. Kidabion®, which was launched in Poland 2007, continued to show dynamic growth. Sales of the multivitamin product for children increased by 27%, confirming its position as the market leader. Sales of Femibion® climbed 61% to € 3.8 million and those of Nasivin® rose 23% to € 5.8 million in Poland. We also grew strongly in other eastern European countries, including the Czech Republic (by 31% to € 4.0 million), Hungary (by 32% to € 4.9 million) and Slovakia (by 6.3% to € 2.4 million).

Global expansion

In Venezuela, we solidified our strong position. Apart from the success of Cebion®, sales of which grew by 27% to € 7.9 million, sales of the fish oil product Maxepa® for cardiovascular care surged again, rising 51% to € 5.7 million. Both products expanded their market leadership positions. Total sales in Venezuela grew by 27% to € 19 million, despite strong negative currency effects.

In India, sales grew by 47% to € 6.6 million despite currency effects. Nasivin® accounted for more than one-half of sales. This successful performance was driven by a dedicated sales force, which we established in 2008.

Sales in India soar by 47% despite substantial currency effects.

The Consumer Health Care division has been present in China since 2007 with the multivitamin syrup Kidabion®. We have meanwhile expanded distribution to five provinces and 12 major cities. In order to further expand the business in this key growth market, we established a legal entity based in Shanghai on January 1, 2009.

Strong brands delivering value

In difficult markets and economically uncertain times, strong brands that consumers trust are more valuable than ever before. Our strategy is succeeding: Sales of Nasivin® grew by 39% to € 46 million in 2008. Sales of Kytta® soared by 75% to € 15 million. Bion®3 also posted strong growth of 24% to € 44 million, as did Femibion®, which grew 32% to € 26 million. Only our Seven Seas® brand saw a year-on-year decline in sales of 6.1% to € 42 million due to unfavorable exchange rate movements.

The future strategy builds on the success of our strategic brands, with which we already achieve more than 50% of our global sales.