The Divisions of the Merck Group → 1/4

Merck Serono

→ *Merck Serono* is the largest division of Merck. It markets innovative prescription drugs of chemical and biological origin. The division offers its leading brands in around 150 countries. Merck Serono focuses on highly specialized therapeutic areas such as multiple sclerosis, oncology, fertility, and endocrinology. The division also offers classic branded products in the area of cardiometabolic care, particularly adapted to the medical needs of patients in emerging markets.

Key products by therapeutic area

- **Multiple sclerosis (MS):** REBIF®
- **Oncology:** ERBITUX® (solid tumors)
- **Fertility:** GONAL-F®, PERGOVERIS™, LUVERIS®, OVIDREL®/OVITRELLE®, CRINONE®, CETROTIDE® (infertility treatment)
- **Endocrinology:** SAIZEN® (growth disorders), SEROSTIM® (HIV-associated wasting), EGRIFTA® (HIV-associated abdominal lipohypertrophy), KUVAN® (metabolic disorder hyperphenylalaninemia)
- **CardioMetabolic Care:** CONCOR® franchise (cardiovascular diseases), GLUCOPHAGE® franchise (type 2 diabetes), EUTHYROX® (thyroid disorders)

Key developments in 2011

- Sales of ERBITUX® rise 4.3% to € 855 million, REBIF® sales increase by 1.4% to € 1,691 million
- Extended indication of REBIF® to treat patients with early signs of multiple sclerosis approved in Europe
- Application to extend the indication of ERBITUX® to first-line therapy of advanced or metastatic non-small cell lung cancer in patients with high EGFR expression submitted again in the EU
- Following negative feedback from the drug regulatory authorities in the United States and the EU, Merck Serono decides not to pursue further the worldwide approval process for cladribine tablets
- All rights for safinamide returned to Newron as part of the review and reprioritization of the R&D pipeline
- Launch of three new pre-filled pens for the self-administration of GONAL-F®, LUVERIS® and OVIDREL® in select markets

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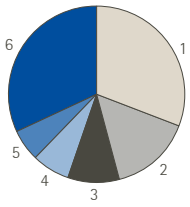
Growth also thanks to classic products

Sales of the Merck Serono division increased slightly over 2010. More than half of this growth was attributable to the three top-selling products in our CardioMetabolic Care portfolio.

The Merck Serono division increased total revenues by 2.9% to € 5,920 million in 2011. Sales rose nominally by 2.9% as well, with foreign exchange rates and divestments exerting a negative impact. Organic growth amounted to 5.1%. The classic branded products from the Glucophage® and Concor® franchises as well as our thyroid products were responsible for more than half of the sales growth driven by emerging markets. Our five top-selling biopharmaceuticals – Rebif®, Erbitux®, Gonal-f®, Saizen®, and Serostim® – generated 60% of sales. Rebif®, our drug to treat relapsing multiple sclerosis, was once again our leading product with sales of € 1,691 million (+1.4%). Erbitux®, our targeted cancer therapy, achieved sales of € 855 million (+4.3%).

Our five top-selling drugs by sales in 2011

€ million / % of divisional sales



1	Rebif®	1,691	31 %
2	Erbitux®	855	15 %
3	Gonal-f®	526	9 %
4	Concor® franchise	397	7 %
5	Glucophage® franchise	346	6 %
6	Other products	1,749	32 %

Operating result declines due to one-time effects

At € 356 million, royalty, license and commission income was higher than in 2010. Gross margin increased slightly to € 4,888 million (+2.0%). Research and development expenses increased by 5.0% to € 1,225 million. The operating result declined by 46% to € 304 million owing to one-time write-downs totaling € 322 million and additional one-time expenses. The largest single effect was the asset impairment of our biotech production plant in Corsier-sur-Vevey (Switzerland) amounting to € 165 million owing to overcapacity. Exceptional items amounted to € 25 million mainly due to a gain of € 19 million in connection with the divestment of Théramex to Teva in 2010. This gain relates to milestone payments for the transfer of distribution rights to Théramex products in a number of countries, including Spain and Brazil. Return on sales (ROS) declined to 5.1%; underlying free cash flow decreased by 7.8% to € 1,205 million.

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Merck Serono | Key figures

€ million	2011	2010	Δ in %
Total revenues	5,920	5,754	2.9
Gross margin	4,888	4,793	2.0
R&D	1,225	1,167	5.0
Operating result	304	565	–46
Exceptional items	25	69	–63
Free cash flow	1,475	1,298	14
Underlying free cash flow	1,205	1,308	–7.8
ROS in %	5.1	9.8	

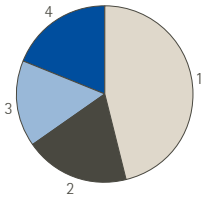
Double-digit sales growth in Latin America

Asia and Latin America drive growth

Europe was once again Merck Serono's top-selling region in 2011, accounting for nearly half of the division's sales, or € 2,545 million. The 3.3% decline was due mainly to the divestment of the Théramex women's health business in 2010. Despite negative exchange rate movements, sales in North America increased by 2.6% to € 1,063 million, mainly thanks to the good performance of Rebif®. Sales in Latin America rose by 11% to € 897 million mainly as a result of the strong growth of our CardioMetabolic Care products and Erbitux®. Geographically, Asia accounted for the largest share of the division's sales growth and recorded a 16% increase in sales to € 865 million. However, this rise was largely due to lower year-earlier sales in China resulting from a change in our local distribution strategy in the third quarter of 2010.

Merck Serono | Sales by region

€ million / % of divisional sales



1	Europe	2,545	46%
2	North America	1,063	19%
3	Latin America	897	16%
4	Asia, Africa, Australasia	1,059	19%

Oncology

The targeted oncology drug Erbitux® (cetuximab) is currently approved for use in colorectal cancer in 90 countries and in head and neck cancer in 88 countries. It is used as a standard treatment in combination with chemotherapy for all lines of therapy or as a monotherapy for pretreated patients in epidermal growth factor receptor (EGFR)-expressing, KRAS wild-type metastatic colorectal cancer (mCRC). In addition, the monoclonal antibody is a standard first-line therapy for the treatment of recurrent and/or metastatic squamous cell carcinoma of the head and neck (SCCHN) in combination with platinum-based chemotherapy,

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as well as in combination with radiotherapy for locally advanced head and neck cancer. We are exploring further indications in additional studies. Sales of Erbitux® rose by 4.3% to € 855 million in 2011.

In the first half of 2011, we sustained a decline in sales in Japan. This was attributable to increased competitive pressure and the introduction of the KRAS biomarker test, which, in line with our commitment to personalized cancer therapy, was introduced after label expansion into first-line metastatic colorectal cancer. As of the third quarter, sales in Japan began to stabilize and then to recover slowly. Sales in the rest of Asia as well as Latin America rose markedly; Europe also saw slight growth.

Erbitux® for lung cancer: Indication extension submitted in the EU

In March, we submitted an indication extension application to the European Medicines Agency (EMA). The application relates to the indication for Erbitux® in combination with standard first-line platinum-based chemotherapy in patients with advanced or metastatic non-small cell lung cancer (NSCLC) with high epidermal growth factor receptor (EGFR) expression. We have established the latter as a predictive biomarker for Erbitux® in the disease. In 2009, the Committee for Medicinal Products for Human Use (CHMP) of the EMA previously adopted a negative opinion on the use of Erbitux® in NSCLC.

Multiple Sclerosis

Continued growth of Rebif® sales despite new competition

With Rebif® (interferon beta-1a), we offer a leading drug for the treatment of relapsing multiple sclerosis (MS). Rebif® is registered in more than 90 countries. According to estimates, around 2 million people suffer from MS worldwide. In spite of the availability of a new oral drug on the market, the sales development of Rebif® remained satisfactory, increasing slightly by 1.4% to € 1,691 million in 2011. With sales of € 773 million, North America was, for the first time, our largest market for Rebif®. Sales grew by 2.9% over 2010. In Europe, sales of Rebif® were slightly below the previous year's level and totaled € 742 million (–1.4%). The highest sales were achieved in Germany and Italy, where we recorded growth rates of 6.8% and 2.7%, respectively. In Latin America, sales increased by 3.2% to € 111 million; in Asia, Africa, Australasia, growth amounted to 14%. The human serum albumin-free formulation of Rebif® is now available in 40 countries around the world. We launched this product, which has improved injection tolerability, in 2007. After having evaluated feedback from the U.S. Food and Drug Administration (FDA), we decided not to pursue registration in the United States any longer.

As of the end of 2011, roughly 30,000 patients outside of the United States were using Rebismart™, the only electronic injection device in MS. Launched in 2009, Rebismart™ allows Rebif® patients to customize their injection settings, and an electronic injection history also enables active adherence management.

Merck Serono is actively supporting the MS community. For example, with the digital platform "UniteMS.net", we created an international social MS network. We also set up the Web portal "MS World Council" especially for health care professionals in 2011. We are also involved in several collaborations designed to advance research into MS, such as our collaboration with Fast Forward, a not-for-profit organization established by the American National Multiple Sclerosis Society.

Based on feedback from the regulatory authorities in the EU and the United States, we decided in June to not pursue further the worldwide approval process for cladribine tablets. Attempting to fulfill the requirements of the European Medicines Agency and the FDA would have necessitated a new, multi-year clinical trial program. In Australia and Russia, where cladribine tablets were registered under the brand name Movectro®, we discontinued market supply of the product in close coordination with the authorities.

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Fertility

We are a global leader with our portfolio of medicines to treat infertility. Merck is the only company that offers recombinant versions of the three main reproductive hormones. The Fertility business unit increased its sales in 2011 by 6.1% to € 697 million and expanded its market share. Europe accounted for nearly half our sales, which remained at the previous year's level. We recorded double-digit growth rates in Asia, Africa, Australasia and Latin America, while sales declined in North America.

Gonal-f® shows strong growth in Asia, Africa, Australasia

Gonal-f® (follitropin alfa for injection) is a recombinant form of natural follicle-stimulating hormone (FSH). It is approved in more than 100 countries and is the world's leading fertility drug. Sales of this product increased by 4.3% to € 526 million thanks to strong, mainly organic growth of 18% in Asia, Africa, Australasia. Sales in both China and Japan grew by around one-third. In Europe, which is our top-selling region for Gonal-f®, sales increased slightly. In North America, sales of Gonal-f® fell by 6.4%, mainly owing to a decrease in the generally declining U.S. market.

Cetrotide® is a medication used to prevent premature ovulation. The use of this class of drugs (gonadotropin-releasing hormone antagonists) is increasing and Cetrotide® benefited from this trend. Sales increased by 32% to € 50 million. Ovidrel®/Ovitrelle® is the only recombinant version of the natural hormone hCG. It is used to trigger follicle maturation and ovulation and generated a 10% increase in sales to € 50 million, mainly thanks to good growth outside of Europe. Our combination treatment Pergoveris™ is used to stimulate follicular development in infertile women with severe luteinizing hormone (LH) and follicle-stimulating hormone (FSH) deficiency. Worldwide sales, which were attributable almost exclusively to Europe, declined by 7.5% to € 29 million.

Three new injection devices expand options for patients

We expanded our range of user-friendly injection devices in 2011 to include three pre-filled pens for the self-administration of the liquid formulations of Gonal-f®, Luveris® (lutropin alfa; recombinant luteinizing hormone) and Ovidrel®. The new pens are approved in Europe, Australia, New Zealand and Canada, and market launches are ongoing.

Endocrinology

The specialized drugs and user-friendly injection devices offered by the Endocrinology business unit can help improve the lives of patients with endocrine and metabolic disorders. Sales increased by 8.0% to € 342 million, based on growth in all regions. Our recombinant human growth hormone Saizen® is approved in around 80 countries for the treatment of a variety of diseases. According to estimates, the incidence of growth hormone deficiency in children is between 1 in 4,000 and 1 in 10,000. Non-childhood-related adult growth hormone deficiency can also be a significant problem which affects 3 in 10,000 each year.

Saizen® generated sales of € 225 million, which was 0.5% less than in the previous year. We nearly offset a decline in prices in several regions of the world (United States, Latin America, Europe) with good volume growth in almost all countries where the product is marketed. At € 105 million, sales in Europe were slightly lower (–1.6%) than in 2010.

Since 2007, around 30,000 patients have used our electronic injection device Easypod™ for the administration of Saizen®. In 2011, we introduced in select markets Easypod™ Connect software, a new approach to monitoring patients' adherence to Saizen® injected using Easypod™.

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Significant sales growth for Kuvan®

Kuvan® (sapropterin) is the first drug approved in Europe for treatment of hyperphenylalaninemia (high levels of phenylalanine in the blood) in patients with the genetic metabolic disorder phenylketonuria (PKU) or a deficiency of the key coenzyme tetrahydrobiopterin (BH4). According to estimates, around 50,000 people are affected in Europe; 20% to 50% of PKU patients could benefit from treatment with Kuvan®. By launching Kuvan® in new markets and expanding the number of patients, we increased global sales of the product by 72% to € 34 million.

Since the registration of Egrifta® (tesamorelin for injection), a registered trademark of Theratechnologies Inc., in the United States at the end of 2010 as a therapy for reducing excess abdominal fat in HIV patients with lipodystrophy, we now offer two drugs for the treatment of HIV-related diseases. The other product Serostim® is used in the United States to treat patients suffering from HIV-associated wasting. Sales of our two drugs used in HIV totaled € 82 million (+17%).

CardioMetabolic Care and General Medicine

The CardioMetabolic Care and General Medicine business unit comprises our drugs for treating diabetes, cardiovascular diseases and thyroid disorders, as well as other globally and regionally marketed products. Sales increased by 1.8% to € 1,976 million. Adjusted for the sales of our Théramex subsidiary, which we divested in 2010, growth amounted to 6.5%. We continued to grow especially in emerging markets by making full use of our medical expertise in conducting intensive life-cycle management programs for our products. In this way we were also able to limit the effects of generic competition in mature markets.

Concor® performs strongly in emerging markets

The branded Concor® products such as Concor®COR and Lodoz®, which contain the active ingredient bisoprolol, achieved sales of € 397 million, which was 6.4% more than in 2010. We succeeded in maintaining sales at a virtually consistent level in France, our top-selling market, despite strong generic competition. At the same time, we achieved strong sales gains in the growth markets of Asia and Latin America. In 2011, we launched Concor AM®, a combination product containing two complementary active ingredients: the beta-blocker bisoprolol and the calcium channel blocker amlodipine. We launched Concor AM® in Hungary in 2011. Launches in additional markets in Europe and Latin America will follow in 2012.

Globally, around 366 million people have diabetes, and the prevalence of this disease is rising. The active ingredient metformin, which is contained in our product Glucophage®, remains the drug of choice for first-line treatment of type 2 diabetes. More than seven million patients worldwide rely on our oral metformin products to treat this condition. The branded products from the Glucophage® range generated sales of € 346 million – an increase of 9.6%. Performance in growth markets was particularly dynamic. Sales of the Glucophage® range rose by 44% in Asia to € 100 million and by 18% in Latin America to € 94 million. We recorded sales declines in Europe because at times we reached our production capacity limits.

Drugs to treat thyroid disorders: Sales increase in China

Merck is the world's largest supplier of medicines to treat thyroid disorders. Sales of our key product, the thyroid hormone Euthyrox®, increased by 19% to € 175 million. Sales of all Merck thyroid products grew by 17% to € 199 million. Emerging markets also drove growth in this field. For instance, sales in China increased by 69% to € 20 million. This market offers tremendous potential as around 90 million people in China have thyroid disorders yet only 2% of them currently receive drug therapy.

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Thanks to their good competitive position in key markets outside of Europe, our other products generated sales of € 1,034 million. Sales of the Neurobion® range increased by 10% to € 198 million. Neurobion® is a multivitamin to treat and prevent vitamin B deficiency. Neurobion® products are available in more than 70 countries.

Status of our innovative compounds

Therapeutic area	Compound	Indication	Status
Oncology		Non-small cell lung cancer (NSCLC)	EU: filed
		Adjuvant colorectal cancer[2]	Phase III
	Erbitux® (cetuximab, anti-EGFR monoclonal antibody)[1]	Gastric cancer	Phase III
	Cilengitide (integrin inhibitor)	Glioblastoma (brain tumor)	Phase III
	Stimuvax® (cancer immunotherapy)[3]	Non-small cell lung cancer (NSCLC)	Phase III
		Head and neck cancer (SCCHN)	Phase II
	Cilengitide	Non-small cell lung cancer (NSCLC)	Phase II
		Metastatic colorectal cancer (mCRC)	Phase II
	Anti-integrin monoclonal antibody (DI17E6)	Metastatic prostate cancer (mCRPC)	Phase II
	Pimasertib (AS703026/MSC1936369B, MEK inhibitor)	Solid tumors and hematological malignancies	Phase I
	Novel combinations of pimasertib with one of two PI3K inhibitors from sanofi-aventis U.S. Inc.[4]	Solid tumors	Phase I
	MEK inhibitor (AS703988/MSC2015103B)	Solid tumors	Phase I
	c-Met kinase inhibitor (EMD1214063)[5]	Solid tumors	Phase I
	NHS-IL12 (cancer immunotherapy)[6]	Solid tumors	Phase I
Multiple Sclerosis	Human serum albumin-free formulation of Rebif®	Treatment of patients with early signs of MS	EU: approved
	ONO-4641 (oral S1P receptor modulator)	MS	Phase II
	ARX 424 (long-acting interferon)	MS	Phase I
	ATX-MS-1467 (immune tolerance therapy)[7]	MS	Phase I
	Extended-release formulation of interferon beta-1a[8]	MS	Phase I
	Plovamer (PI-2301, second-generation peptide copolymer)	MS	Phase I
	DI Fc-IFN beta variant (long-acting interferon)	MS	Phase I
Rheumatology	Atacicept (anti-BLyS/anti-APRIL fusion protein)[9]	Systemic lupus erythematosus (SLE)	Phase II
		Cartilage injury	Phase II
	Fibroblast growth factor (FGF) 18[9]	Osteoarthritis	Phase I
Endocrinology	Kuvan® (sapropterin)	PKU in children under the age of 4[10]	Phase III

[1] Collaboration between Merck KGaA, Darmstadt, Germany, and ImClone LLC, a wholly-owned subsidiary of Eli Lilly and Company. Erbitux® is a trademark of ImClone, used under license by Merck
[2] Study sponsored and coordinated by the Fédération Francophone de Cancérologie Digestive (FFCD)
[3] Exclusive worldwide licensing rights acquired from Oncothyreon Inc.
[4] Combined with PI3K/mTOR inhibitor (SAR245409), conducted by Merck, or combined with PI3K inhibitor (SAR245408), conducted by sanofi-aventis U.S. Inc.
[5] Scientific collaboration with M. D. Anderson Cancer Center
[6] Sponsored by the National Cancer Institute (NCI), USA
[7] Collaboration with Apitope Technology (Bristol) Ltd.
[8] Collaboration with Flamel Technologies S.A.
[9] In-licensed from ZymoGenetics, Inc., a wholly-owned subsidiary of Bristol-Myers Squibb Company
[10] Phase IIIb study as part of the EMA's requirements for registration

NSCLC: Non-small cell lung cancer
SCCHN: Squamous cell carcinoma of the head and neck
mCRC: Metastatic colorectal cancer
mCRPC: Metastatic castration-resistant prostate cancer
S1P: Sphingosin-1 phosphate
PKU: Phenylketonuria

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Opportunities in Research & Development

At € 1,225 million, research and development spending in 2011 was 5.0% higher than in 2010. This was partly due to the continued high number of costly trials in late-stage clinical development. We operate research centers in Europe, the United States and Asia. This allows us to optimally exploit strong local networks and ensures diversity. The pipeline comprises eleven programs in Phase I clinical trials, seven in Phase II and five in Phase III.

Oncology, multiple sclerosis and immune system-related disorders are our key areas of focus. In addition, we continue to conduct product development in Fertility and Endocrinology. We intend to increasingly apply our strengths in biotechnology to immune-related diseases and explore new indications in this area.

In order to balance our presence globally, we are increasing our R&D activities in the United States and China. We expanded our engagement in the Beijing area through a strategic partnership with Pharmaron and opened an R&D laboratory on the Pharmaron campus in August 2011. As of December 31, 2011, around 2,850 people worked for the research and development function of the Merck Serono division.

New organization

To meet the growing demands on pharmaceutical companies, we are realigning our R&D organization. Research and Early Development was separated from late-stage Development and Medical. The transition between the two takes place at "proof of confidence," when the available data is sufficient to justify significant investment in further clinical development. Our aim is to create an agile, flexible and innovative organization for research and early-stage development, strongly supported by scientific networks and focusing on translational science and medicine. In late-stage clinical development, we are aiming to ensure that standardized processes run reliably, effectively and in compliance with the highest quality standards in order to enhance our chances of satisfying the requirements of regulatory authorities for drug approval.

We worked further to build a collaborative scientific enterprise in 2011, investing specifically in partnerships with pharmaceutical companies, small biotech firms as well as academic institutions. Having the appropriate tools is one of the levers in the discovery of new medicines and we are therefore engaging in new technologies.

Strong scientific network

In 2011, we further expanded our relationship with Ablynx and entered into a third agreement to co-discover and co-develop Nanobodies® against two targets in osteoarthritis. Nanobodies® are a novel class of antibody-based therapeutic proteins that combine the advantages of antibodies with those of small-molecule drugs. The agreement with F-Star is another example of our engagement in new technologies. Here our intention is to discover new antibody-derived therapeutics against inflammatory disease targets, using F-Star's modular antibody technology. We initiated our relationship with F-Star in 2010 through Merck Serono Ventures, our corporate venture capital fund.

In 2011, we set up the Merck Serono Israel Bioincubator Fund, a strategic and corporate initiative targeting Israeli biotechnology start-ups. The fund will offer both seed financing and the opportunity to use certain labs at Merck Serono's Israeli R&D center. We will commit a total of € 10 million to the program over a seven-year period.

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Oncology: Strong data underscore the potential of Erbitux®

The results of the retrospective analysis of data from the Phase III CRYSTAL trial in metastatic colorectal cancer (mCRC) were published in 2011. The new analysis examined the benefits of first-line treatment with Erbitux® in combination with standard chemotherapy (FOLFIRI) in KRAS wild-type patients, dependent on metastatic site. Results showed that in patients with advanced metastatic disease that had spread beyond the liver, the additional administration of Erbitux® compared to chemotherapy alone led to a significant increase in overall survival of more than five months in palliative treatment.

In 2011, a further analysis of the randomized Phase II OPUS trial demonstrated an association between early tumor shrinkage and long-term median overall survival of more than two years in metastatic colorectal cancer patients with KRAS wild-type tumors who were treated with Erbitux® in combination with the standard chemotherapy FOLFOX. These results confirm earlier outcomes of a similar analysis of the pivotal Phase III CRYSTAL trial.

In 2011, recruitment was completed into the pivotal Phase III EXPAND clinical trial investigating the efficacy of Erbitux® in patients with advanced gastric cancer. This international study has recruited more than 870 patients since commencing enrollment in 2008.

Stimuvax® cancer immunotherapy: Development progressing on schedule

Since 2007, we have been studying the efficacy and safety of the cancer immunotherapy Stimuvax® in patients with inoperable stage III non-small cell lung cancer in the pivotal Phase III START trial. We completed patient recruitment in 2011.

Merck Serono entered into two collaboration agreements with Ono Pharmaceutical to strengthen its multiple sclerosis and cancer franchises. The oncology agreement provides Ono with rights to co-develop and co-market Stimuvax® in Japan.

We completed patient enrollment into the global pivotal Phase III clinical study CENTRIC in June. In this trial, we are assessing the safety and efficacy of cilengitide in glioblastoma, the most aggressive type of brain tumor. Cilengitide is the first integrin inhibitor in oncology to have entered Phase III clinical development.

Early-stage pipeline: Priority given to the most promising projects

In December 2010, we signed a worldwide research and development agreement with sanofi-aventis U.S. Inc. This collaboration provides mutual access to experimental compound combinations. The novel combinations include one of our MEK inhibitors as well as two early-stage development compounds from sanofi-aventis. The trials in solid tumors are in Phase I.

Overall, we are investigating five projects in Phase I trials in patients with solid tumors and hematological malignancies. A further four Phase II trials are underway in head and neck cancer, non-small cell lung cancer, colorectal cancer as well as prostate cancer.

In order to be able to forge ahead with the most promising projects, we intend to terminate or transfer to partners projects with risk-benefit profiles that do not meet our requirements. We therefore discontinued clinical development of Erbitux® in triple-negative breast cancer as well as of the immunomodulator IMO-2055. Clinical development of one of the two c-Met kinase inhibitors in Phase I was also terminated based on the available comparative data.

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Multiple sclerosis: Indication extension for Rebif® approved in the European Union

In Neurodegenerative Diseases, our focus is on new therapeutic options for patients with multiple sclerosis. In November, the Committee for Medicinal Products for Human Use of the European Medicines Agency (EMA) issued a positive opinion on our application to extend the indication for our MS drug Rebif®. EU marketing authorization was granted in January 2012. The indication extension relates to the use of Rebif® in patients who have experienced a single demyelinating event, an early sign of the disease, and who are at high risk of converting to MS. The marketing authorization application submitted in June was based on the results of the two-year REFLEX study with over 500 patients. Rebif® significantly delayed the onset of MS in these patients. A three-year double-blind extension of the REFLEX study, called REFLEXION, is currently ongoing in order to provide long-term follow-up data. We also submitted marketing authorization applications for the new indication in Canada and Switzerland.

Compounds to treat MS added to pipeline

We further expanded our portfolio of compounds for the treatment of MS, acquiring from Peptimmune the global exclusive rights to plovamer (PI-2301), a second-generation peptide copolymer thought to enhance the regulatory response of the immune system, which has successfully completed Phase Ib trials in MS. In addition, we were granted a license by Ono Pharmaceutical to develop and commercialize ONO-4641, an oral investigational sphingosine-1-phosphate (S1P) receptor modulator, in Phase II in MS, worldwide except in Japan, Korea and Taiwan.

Parkinson's disease: Rights to safinamide returned

In October, we announced our decision to return all rights for safinamide in Parkinson's disease and other therapeutic applications to our partner Newron Pharmaceuticals effective April 2012. Our decision was made as part of the ongoing review and re-prioritization of our R&D pipeline. In Merck Serono's view, safinamide has a more limited market potential than originally expected. We fully wrote off the book value of safinamide by the end of the second quarter of 2011. We will meet our contractual and ethical commitments regarding the ongoing clinical development program for safinamide in Parkinson's disease and will work with Newron to conduct an appropriate transfer of the program to Newron. This applies in particular to the two Phase III studies MOTION and SETTLE, for which patient recruitment was completed in the summer. We will continue to pursue innovative therapeutic options in the field of neurodegenerative diseases above and beyond MS and are currently investigating suitable indications.

Fertility: Advancing the science of infertility treatment

Up to € 1 million granted to promote applied fertility research projects

The objective of our Fertility research and development work is to help infertile couples in every phase of the reproductive cycle from follicular development to pregnancy. We focus on drugs, delivery technologies and support services for the benefit of patients. Our innovative drugs address unmet medical needs and our application devices offer patients ease of use. Our research efforts concentrate on non-invasive methods to assess embryo quality and on the successful implantation of the embryo into the uterus.

Complementary to our own activities, we are supporting applied fertility research projects through the Grant for Fertility Innovation program. In 2011, for the second time, we awarded up to € 1 million to support five innovative projects with the same common goal: to improve the chances for couples to conceive.

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Endocrinology: Expanding the understanding of our drugs

The aim of our Endocrinology research and development work is to offer patients with growth disorders and selected metabolic diseases new therapeutic options. We also want to continuously enhance the understanding of the products in our portfolio. In the PKU area we started the Phase IIIb trial SPARK in June. It is investigating the effects of Kuvan® in 50 European PKU patients younger than four years of age, for whom the drug is not yet approved. Additionally, with KAMPER, a multinational observational registry which started in 2009, we are studying the long-term safety of Kuvan®. Patient recruitment is still underway. For our growth hormone Saizen® we are using a two-pronged strategy in select countries to investigate how patients can achieve their full outcome potential. In the multinational observational study ECOS, which began in February, we are assessing patient adherence and its impact on treatment outcomes. The study aims to recruit and monitor at least 1,000 pediatric patients receiving Saizen® therapy via the Easypod™ injection device over a period of up to five years. In the pharmacogenetic program PREDICT, we are studying genetic markers that correlate with response to growth hormone treatment.

Rheumatological diseases: Treating lupus and damaged cartilage

Our research and development work in Rheumatology is centered on molecules that modulate key pathogenic mechanisms. We are investigating the recombinant protein atacicept as a potential treatment for systemic lupus erythematosus (SLE) in a clinical trial. SLE is a chronic autoimmune disease that primarily affects women. As recommended by the Independent Data Monitoring Committee of the trial, the high-dose arm was discontinued in February because the risk-benefit profile for this group of patients was considered unfavorable. The study is being continued with the lower-dose and placebo groups.

We reset the SLE program to Phase II since the optimum dose regimen for Phase III trials still needs to be identified. In 2011, we started a new Phase I study in lupus nephritis (LN), a particularly severe form of SLE affecting the kidneys. Following a fatal cardiovascular event, the study was discontinued. The causality between this fatal event and the administration of atacicept is still being investigated.

Second Phase I trial completed for FGF 18 for osteoarthritis of the knee joint

Fibroblast growth factor 18 (FGF 18) is another recombinant protein in our rheumatology pipeline. Thanks to its novel mechanism of action, it could be the first disease-modifying treatment for osteoarthritis and the repair of damaged cartilage. We successfully completed the second Phase I trial of this agent in patients with osteoarthritis of the knee joint. Phase II trials are scheduled to begin in 2012. We are also investigating the efficacy of FGF 18 in the treatment of knee cartilage injury in an ongoing Phase II study.