MERCK SERONO

Merck Serono is the largest division of Merck. It markets innovative prescription drugs of chemical and biotechnological origin. The division offers its leading brands in around 150 countries. Merck Serono focuses on highly specialized therapeutic areas such as Neurodegenerative Diseases, Oncology, Fertility, Endocrinology and Rheumatology.

KEY PRODUCTS BY THERAPEUTIC AREA

- Oncology: Erbitux® (solid tumors)
- Neurodegenerative Diseases: Rebif®, Movectro® (multiple sclerosis)
- Fertility: Gonal-f®, Pergoveris™, Luveris®, Ovitrelle®, Crinone®, Cetrotide® (infertility treatment)
- Endocrinology: Saizen® (growth hormone disorders), Serostim® (HIV-associated wasting), Kuvan® (metabolic disorder hyperphenylalaninemia), Egrifta™ (HIV-associated lipodystrophy)
- CardioMetabolic Care: Concor® franchise (cardiovascular diseases), Glucophage® franchise (type 2 diabetes), Euthyrox® (thyroid disorders)

KEY DEVELOPMENTS IN 2010

- Sales of Erbitux® rise by 18% to EUR 820 million, Rebif® sales increase by 8.6% to EUR 1,668 million
- Russian and Australian regulatory authorities approve cladribine tablets as the world's first oral disease-modifying treatment for multiple sclerosis (brand name: Movectro®)
- The Committee for Medicinal Products for Human Use of the EMA adopts a final negative opinion regarding the marketing authorization application for cladribine tablets in January 2011. In the United States, the FDA accepts the application for review; FDA feedback on the application is expected by the end of February 2011
- The Japanese drug regulatory authorities approve extended usage for Erbitux® in combination with chemotherapy for first-line treatment of metastatic colorectal cancer (KRAS wild-type tumors)
- Following a suspected unexpected serious adverse reaction we temporarily suspended all studies with the cancer immunotherapy Stimuvax® in March. Phase III trials resumed in non-small cell lung cancer in June
- Egrifta™ approved in the United States to reduce excess abdominal fat in HIV patients with lipodystrophy

STRONG GROWTH THANKS TO BIOTECH MEDICINES

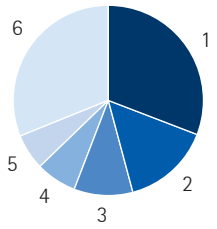
Sales by the Merck Serono division grew far more strongly than the forecasted average for the pharmaceutical industry. Nearly two-thirds of this growth is attributable to the biopharmaceuticals Rebif® and Erbitux®.

Five top-selling biopharmaceuticals account for 61% of sales

In 2010, the Merck Serono division increased total revenues by 7.6% to EUR 5,754 million. Sales increased by 8.3%, with positive currency effects accounting for 2.6% of the increase. This excellent growth, which exceeded the sector average of 4% to 5% estimated by IMS Health, was once again due to the success of our biopharmaceuticals. We generated EUR 3,288 million or 61% of our sales with our five top-selling biopharmaceuticals Rebif®, Erbitux®, Saizen®, Gonal-f® and Serostim®. Rebif®, a treatment for relapsing-remitting multiple sclerosis, was once again the top-selling product, with sales increasing by 8.6% to EUR 1,668 million. Erbitux®, our targeted cancer therapy, posted another double-digit increase in sales, which rose by 18% to EUR 820 million. In March, Erbitux® received approval in the key market of Japan for extended usage in combination with chemotherapy for the first-line treatment of metastatic colorectal cancer (KRAS wild-type tumors). Cladribine tablets (brand name Movectro®) were approved in Russia in July, becoming the world's first oral disease-modifying treatment for relapsing-remitting multiple sclerosis. Approval in Australia followed in September. In November, the U.S. Food and Drug Administration granted approval of Egrifta™ (tesamorelin for injection) to reduce excess abdominal fat in HIV-infected patients with lipodystrophy.

Our five top-selling drugs by sales in 2010

EUR million / % of divisional sales		
1 Rebif®	1,668	31%
2 Erbitux®	820	15%
3 Gonal-f®	504	9%
4 Concor® franchise	373	7%
5 Glucophage® franchise	316	6%
6 Other products	1,727	32%



At EUR 344 million, royalty, license and commission income was slightly below the previous year's level. In comparison with 2009, the division's gross margin increased by 6.9% to EUR 4,793 million. Due to strong exchange rate effects and investments in new products and emerging markets such as China, marketing and selling expenses were 10% higher than in 2009. Research and development costs declined moderately by 1.4% to EUR 1,167 million. In total, non-recurring expenses were lower than in 2009. The largest single non-recurring item was the impairment loss for safinamide (see page 19). Overall, the operating result improved by 59% to EUR 565 million. Return on sales (ROS) increased to 9.8% in 2010. Underlying free cash flow grew by 51% to EUR 1,308 million.

Merck Serono | Key figures

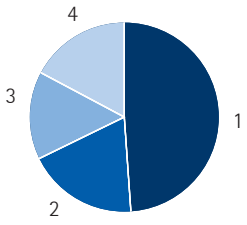
EUR million	2010	2009	Δ in %
Total revenues	5,754	5,345	7.6
Gross margin	4,793	4,485	6.9
R&D	1,167	1,184	–1.4
Operating result	565	355	59
Exceptional items	69	–40	–
Free cash flow	1,298	864	50
Underlying free cash flow	1,308	867	51
ROS in %	9.8	6.6	

Growth driven by Asia, Africa, Australasia

As in the previous year, Europe was the division's top-selling region in 2010. Around one-half of the division's sales were achieved here. European sales increased by 2.9% to EUR 2,632 million. Our largest market within Europe was France, where sales totaled EUR 514 million. Sales there fell by 3.5%, due in part to generic competition faced by our CardioMetabolic Care business. Sales in Germany, our second-largest European market, stagnated at EUR 497 million (+0.1%) as a consequence of a restrictive health care policy. In Italy and Spain, sales increased by 7.1% and 1.8%, respectively, to EUR 308 million and EUR 294 million, putting them nearly on par with each another. Russia and Turkey were two examples of smaller markets that posted strong growth of 36% and 16%, respectively. However, sales in Greece declined by 13% because of the impact of the financial crisis on the health care sector.

Merck Serono | Sales by region

EUR million / % of divisional sales		
1 Europe	2,632	49%
2 North America	1,035	19%
3 Latin America	809	15%
4 Asia, Africa, Australasia	932	17%



Double-digit sales growth in Latin America

In North America, sales increased 9.4% to EUR 1,035 million, mainly due to the good performance of Rebif® and positive currency influences. Sales in Latin America increased by 14% to EUR 809 million. Brazil, our largest market in this region, posted sales growth of 36% to EUR 286 million. Mexico and Argentina also developed well, increasing sales by 22% and 44%, respectively. However, sales in Venezuela dropped by 54% because of strong currency effects. With sales increasing by 20% to EUR 932 million, the Asia, Africa, Australasia region was the division's geographic growth driver. Our largest market within this region was Japan. Thanks to the success of Erbitux®, sales increased there by 39% to EUR 177 million. With sales of EUR 126 million (+2.4%), China was our second-largest market in the region. We achieved growth of 18% in India, where sales totaled EUR 66 million. Sales climbed by 52% to EUR 39 million in South Africa and by 18% to EUR 60 million in Australia.

Our activities by therapeutic area

	Research	Development	Marketing
Oncology	■	■	■
Neurodegenerative Diseases	■	■	■
Rheumatology	■	■	
Fertility	■	■	■
Endocrinology		■	■
CardioMetabolic Care and General Medicine			■

ONCOLOGY

Our targeted oncology drug Erbitux® (cetuximab) is approved in combination with chemotherapy for all lines of treatment 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 first-line standard for recurrent and/or metastatic squamous cell carcinoma of the head and neck (SCCHN) in combination with platinum-based chemotherapy, as well as in combination with radiotherapy for locally advanced head and neck cancer. Erbitux® is currently approved for use in colorectal cancer in 86 countries and in head and neck cancer in 82 countries around the world. We are exploring further indications in additional studies. Sales of Erbitux® continued on a growth course in 2010, increasing by 18% to EUR 820 million.

Approvals in Japan, Australia and Switzerland

Erbitux® in combination with chemotherapy available in Japan for colorectal cancer in all lines of treatment

In Japan, Erbitux® can now be used in combination with chemotherapy in the first-line treatment of patients with EGFR-expressing, inoperable, advanced or recurrent colorectal cancer carrying the KRAS wild-type gene. The Japanese Pharmaceutical and Medical Devices Agency (PMDA) granted approval of this extended usage for Erbitux® in March 2010 following submission of data from the Phase III CRYSTAL trial. Consequently, Erbitux® is now available for use in combination with chemotherapy for colorectal cancer in all lines of treatment in Japan. In Australia, the Therapeutic Goods Administration (TGA) approved Erbitux® in March 2010 as a first-line treatment in combination with chemotherapy for patients with KRAS wild-type mCRC. In Switzerland, Erbitux® was also approved in 2010 as a first-line treatment option for metastatic colorectal cancer patients with KRAS wild-type tumors. Swissmedic, the Swiss Agency for Therapeutic Products, granted the approval in September 2010.

Erbitux® is the standard of care in KRAS wild-type metastatic colorectal cancer

Merck is a leader in innovative, personalized cancer therapy. We are focused on research to identify biomarkers that will help to select the patients who will benefit the most from a specific drug – as is the case with Erbitux® and the KRAS wild-type status of tumors in patients with metastatic colorectal cancer. An international survey conducted in 2010 showed that KRAS mutation analysis is fast becoming an integral part of the management of mCRC. The survey revealed in addition that Erbitux® is now a standard of care for confirmed KRAS wild-type

mCRC. The share of patients in whom the test is performed in order to determine whether they can benefit from a personalized therapy, such as Erbitux®, increased from 2.5% in 2008 to 66% in early 2010. The results also show that 73% of physicians in Europe already routinely tested KRAS status at diagnosis of metastatic colorectal cancer. Data from two surveys, which were likewise presented in 2010, show that Erbitux® has become a standard of care in the treatment of both locally advanced and recurrent and/or metastatic SCCHN. The results from the survey of 256 specialists in France, Germany, Italy and Spain in the latter indication showed that an Erbitux®-based treatment combination was used in almost 60% of cases in the first-line setting.

NEURODEGENERATIVE DISEASES

Within the Business Unit Neurodegenerative Diseases, we offer Rebif® (interferon beta-1a), one of the leading drugs for the treatment of relapsing-remitting multiple sclerosis (MS). According to estimates, around 2 million people suffer from MS worldwide. Owing to its proven efficacy and favorable risk-benefit profile, Rebif® is a basic treatment for MS and is approved in more than 90 countries. In 2010, sales of Rebif® increased by 8.6% to EUR 1,668 million. The recombinant protein was thus once again our top-selling product and remained the leading MS treatment outside the United States. With sales growing solidly by 6.2% to EUR 752 million, Europe was our strongest region for Rebif®. The largest markets were Germany and Italy, where we recorded growth rates of 6.0% and 8.5%, respectively. With sales of EUR 751 million, North America remained our second-largest market for Rebif®. Sales in this region grew by 11% over 2009. Sales in Latin America increased by 12% to EUR 108 million. In the region Asia, Africa, Australasia, sales increased by 2.2%.
The serum-free formulation of Rebif® with improved injection tolerability is now available in around 40 countries, including all EU member states, Australia, Canada and Switzerland, as well as a number of countries in Asia, Latin America, Africa, and the Middle East. Discussions with the U.S. Food and Drug Administration concerning a potential approval continue. Rebidose™ is the latest addition to our range of user-friendly injection devices for the self-administration of Rebif®. This single-use pen, which is prefilled with Rebif®, was approved in the European Union and Australia. Launched in 2009 as the first electronic injection device of its kind for MS, Rebismart™ is now available in more than 20 countries, including Canada and many EU countries.

Movectro® approved in Russia as the world's first oral disease-modifying drug for MS

Movectro® approved in Russia and Australia as an oral treatment for MS
In July, the Russian regulatory authorities granted marketing approval for cladribine tablets for the treatment of relapsing-remitting multiple sclerosis. This was the world's first approval of an oral disease-modifying therapy for multiple sclerosis. The next approval followed in Australia in September. Cladribine tablets have been available under the trade name Movectro® in both countries since the end of 2010. The approvals are supported by the results of the CLARITY study, which involved 1,326 patients with relapsing-remitting multiple sclerosis. The study results published in the New England Journal of Medicine showed that short-course treatment with cladribine tablets significantly reduced relapse rates, the risk of disability progression, and MRI measures of disease activity at 96 weeks.

We have submitted regulatory applications for cladribine tablets covering around 40 countries worldwide. We resubmitted our regulatory application in the United States in June. The U.S. agency accepted the application for filing in July and granted a Priority Review designation. The FDA informed us in November that it had extended its Priority Review period by three months to February 28, 2011 in order to have more time for a full review of additional information provided under the application. In September, the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) issued a negative opinion regarding the marketing authorization application for cladribine tablets. Since we are convinced of the potential of cladribine tablets as a new therapeutic option for people with multiple sclerosis, we appealed and requested re-examination of this opinion. In January 2011, the CHMP adopted a final negative opinion regarding our marketing authorization application.

FERTILITY

Double-digit increase in sales in important growth markets

The Merck Serono division is the global leader with its portfolio of drugs to treat infertility. We are the only company that offers physicians and patients recombinant versions of the three main reproductive hormones that are important for the treatment of infertility. In 2010, sales by the Business Unit Fertility increased by 6.6% to EUR 657 million. We generated nearly half of our sales in Europe, which remains our largest market. In 2010, sales in Europe were slightly higher than in 2009. We recorded double-digit growth in the regions Asia, Africa, Australasia and Latin America, while sales increased slightly in North America.

Growth of Gonal-f® continues

Gonal-f® (follitropin alfa for injection) is a recombinant form of the natural follicle-stimulating hormone. It is approved in over 100 countries and is the world's leading female fertility drug. The injection device Gonal-f® pen for the self-administration of Gonal-f® is now available in more than 90 countries, including the largest EU markets, the United States and Japan. Sales of Gonal-f® grew by 3.7% to EUR 504 million, primarily as a result of strong growth of 15% in Asia, Africa, Australasia. Positive currency effects were responsible for more than half of the increase in this region. Gonal-f® was additionally approved in Japan in 2009 for the treatment of infertile women with irregular or absent ovulation. Consequently, sales increased sharply in 2010. In North America, Gonal-f® sales remained at the previous year's level in a declining and hotly contested market. In Europe, which accounts for nearly half of our Gonal-f® sales, we stopped the negative trend of 2009 and maintained sales at the previous year's level despite unabated cost containment pressure in the health care sector. In Italy, our largest European market for this product, sales remained just as stable as in France, our second-largest market. Spain is the third-largest market in Europe and is dominated by private payers, who continued to feel the effects of the economic crisis. Consequently, sales of Gonal-f® declined by 4.3%. By contrast, Gonal-f® performed well in the United Kingdom. Sales grew strongly in this market, mainly on an organic basis, increasing 31% over 2009.

Our recombinant combination treatment Pergoveris™ is used to stimulate follicular development in infertile women with severe follicle-stimulating hormone and luteinizing hormone deficiency. It is the first drug to allow the simultaneous administration of the two key hormones for ovarian stimulation in a single subcutaneous injection. Global sales, which are achieved almost exclusively in Europe, increased by 8.4% to EUR 32 million, primarily thanks to growth of 50% in France. Ovidrel®/Ovitrelle® is a recombinant version of the natural hormone hCG and is used to trigger follicle maturation and ovulation. Sales of Ovidrel®/Ovitrelle® grew strongly by 21% to EUR 45 million, thanks to good growth in all regions. Sales of Cetrotide®, a gonadotropin-releasing hormone antagonist used to prevent premature ovulation, also rose sharply by 23% to EUR 38 million.

Grant to promote innovative fertility projects

Merck Serono awards around EUR 1 million to further applied research projects in fertility

In June, Merck Serono announced the first recipients of funds from the Grant for Fertility Innovation. We set up this program for innovation in fertility in order to further medical research in this field. Around EUR 1 million was awarded to five innovative applied research projects that aim to help infertile couples improve their chances of conceiving. In the same month, we presented the results of the largest international study aimed at understanding the decision-making process of couples trying to conceive. The findings can help clarify disparities in fertility rates and reveal barriers that may prevent couples with infertility from seeking medical help. More than 10,000 men and women from 18 countries responded to the survey, which was developed in collaboration with Cardiff University in Wales (United Kingdom).

ENDOCRINOLOGY

Our electronic autoinjector Easypod™ for the self-administration of Saizen® now also available in China

The specialized therapies and user-friendly injection devices offered by the Business Unit Endocrinology can help improve the lives of patients with endocrine and metabolic disorders. Sales increased by 21% over 2009 to EUR 317 million thanks to strong growth in all regions. Our top-selling endocrinology product is Saizen®, a recombinant human growth hormone. Saizen® is approved in 79 countries for indications including the treatment of pediatric and adult growth hormone deficiency, Turner syndrome, growth failure in children associated with chronic renal failure, as well as to treat children born small for gestational age (SGA). According to estimates, growth hormone deficiency affects 330,000 children globally and 90,000 adults in Europe. Sales of Saizen® increased sharply by 18% to EUR 226 million. Our top-selling markets were Europe and North America. Latin America as well as Asia, Africa, Australasia showed strong, double-digit growth, also on an organic basis. The ongoing success of Saizen® was favorably impacted by the high acceptance of our electronic injection device Easypod™, which is now available in around 40 countries, including China, where it was approved in July. In order to make Saizen® even more user-friendly, we developed a ready-to-use liquid formulation that eliminates the need to prepare the powder for injection. Saizen® solution for injection was approved in Canada in April. A decentralized procedure was completed in the European Union in October, allowing national approvals in 18 EU member states in the coming

months. To ensure flexibility in meeting the individual needs of patients, the new formulation is available in cartridges of 6 mg, 12 mg and 20 mg, designed for exclusive use with Easypod™ and our needle-free auto-injector Cool.click™2.

With Kuvan® (sapropterin) for the treatment of hyperphenylalaninemia in patients with either phenylketonuria (PKU), a congenital metabolic disorder, or a deficiency of the key coenzyme tetrahydrobiopterin (BH_4), we began offering the first drug for this orphan disease in Europe in 2009. According to estimates, around 50,000 people are affected in Europe; 20% to 50% of PKU patients could benefit from treatment with Kuvan®, which Merck Serono markets in around 30 countries. In 2010, the product was approved in Switzerland and Croatia as well as a number of countries outside of Europe, including Australia, China (only for BH_4 deficiency), Israel, Mexico and Venezuela. Global sales rose to EUR 20 million.

Egrifta™ approved in the United States

Egrifta™ is the first FDA-approved drug to reduce excess abdominal fat in HIV-infected patients with lipodystrophy

Our drug Serostim® is used in the United States to treat patients suffering from HIV-associated wasting, which is estimated to affect up to 8% of HIV-infected individuals. Sales of Serostim® increased by 8.1% to EUR 70 million.

In November, the U.S. Food and Drug Administration (FDA) approved Egrifta™ (tesamorelin for injection) as the first, and so far only, treatment indicated to reduce excess abdominal fat in HIV-infected patients with lipodystrophy. Egrifta™ was developed by Theratechnologies, a Canadian biopharmaceutical company, and will be marketed in the United States exclusively by our subsidiary EMD Serono.

CARDIOMETABOLIC CARE AND GENERAL MEDICINE

We are expanding our position with CardioMetabolic Care products in many key growth markets

The Business Unit CardioMetabolic Care and General Medicine comprises our drugs for treating diabetes, cardiovascular diseases and thyroid disorders, as well as other products and regional specialties. The interrelationships that exist between many chronic cardiovascular and metabolic diseases are the causes of multiple complex clinical pictures that call for integrated therapeutic approaches. We are continually working to improve our products, for example by developing new dosage forms and strengths.

At EUR 1,888 million, sales by this Business Unit grew by 4.4%. We expanded our position in many dynamic markets. For example, our CardioMetabolic Care products have made us one of the fastest growing pharmaceutical companies in Latin America and Asia. In Latin America we rank among the top 15 pharmaceutical companies. However, price reductions in Europe and generic competition in France, our largest market in terms of sales, had a negative impact. Overall, the decline in sales of beta-blockers was more than offset by higher sales of diabetes and thyroid medicines.

Concor®: Strong performance in growth markets, fierce competition in Europe

Sales of branded Concor® products containing the active ingredient bisoprolol amounted to EUR 373 million. This was 5.3% less than in 2009. One reason was generic competition in France, where sales dropped by 35% to EUR 62 million. Yet in Europe, our largest market for this product group, bisoprolol remains the leading beta-blocker, used in products such as Lodoz® and Concor® COR.

Sales in Venezuela, our largest market in Latin America, suffered an inflation-induced decline of 50% to EUR 11 million.

By contrast, Concor® branded products were successful in growth markets. Sales in Africa, Asia, Australasia grew 30% to EUR 98 million.

Glucophage® franchise continues on a growth course

Seven million patients use oral metformin products from Merck Serono to treat their diabetes

Worldwide, around 285 million people suffer from type 2 diabetes and the number is rising. More than seven million patients worldwide rely on our oral metformin products to treat this condition. Metformin, which is contained in our product Glucophage®, remains the drug of choice for first-line treatment of type 2 diabetes.

The branded products from the Glucophage® franchise generated sales of EUR 316 million – an increase of 8.4%. Slight sales declines in Europe were more than offset by double-digit growth in the markets of Latin America and Asia. In Latin America, Glucophage® is the leading product in the diabetes market. With growth of 34%, sales outperformed the market by six percentage points on a U.S. dollar basis. In addition, product line extensions continued to perform successfully. Sales of Glucophage XR® rose by 21% to EUR 69 million. We had launched a 1000 mg dosage strength of this product in 2009. With Glucovance® 1000 mg/5 mg, a combination of the active ingredients metformin and glibenclamide, we began launching a new dosage strength in 2010.

Thyroid products show good growth

Merck is the world's largest supplier of drugs to treat thyroid disorders. Sales of these products grew by 7.6% to EUR 170 million. Despite generic competition, sales in Europe declined by only 1.3%. By contrast, sales in Latin America increased sharply by 30% and by 3.9% in Asia, Africa, Australasia. Sales of our key product, the thyroid hormone Euthyrox®, increased by 7.7% to EUR 148 million. Approximately 15 million patients in about 90 countries around the world receive treatment with Euthyrox®.

Worldwide, more than 300 million people suffer from hypothyroidism yet not even 20% of them are treated. We want to educate the public and promote optimum treatment of these disorders. Therefore, in May we conducted our second major public awareness campaign together with the International Thyroid Association. Activities took place in 45 countries.

Strong regional performance of other General Medicine products

Due to our good competitive positions in major markets outside Europe, our other General Medicine products, some of which are only sold in certain regions, generated sales of EUR 977 million. This was 5.4% more than in 2009.

RESEARCH AND DEVELOPMENT

At EUR 1,167 million, research and development spending was slightly lower (–1.4%) than in 2009. This decline is due on the one hand to the project delays experienced with Stimuvax® and cladribine tablets, and on the other hand to our successful efforts to optimize cost structures through efficiency enhancement measures. We invested around 20% of the total revenues of the Merck Serono division in R&D, which puts us at an above-average level within the pharmaceutical industry. This is mainly the result of the large number of cost-intensive studies in the final phase of clinical development. The pipeline currently comprises nine projects in Phase III clinical trials, seven in Phase II, and six in Phase I.

Our activities are focused on three areas: oncology, where we are seeking new therapeutic options for colorectal cancer, lung cancer, head and neck cancer, brain tumors, breast cancer and gastric cancer; neurodegenerative diseases, where we are working on new therapies for multiple sclerosis, Parkinson's disease and Alzheimer's disease; as well as rheumatology, which includes the autoimmune disease lupus erythematosus and osteoarthritis. We also continue to conduct research in the field of fertility. As of December 31, 2010, the division had around 3,000 employees working in research and development.

Our most important research centers are Darmstadt, Geneva and Boston. Additionally, we are expanding the Beijing site in order to cover Asia, to facilitate regional clinical trials, and to form local alliances. We plan to invest EUR 150 million and create more than 200 qualified positions here by 2013. The expansion work was completed as planned at the Billerica site, where we invested USD 65 million.

Networks and partnerships help to address challenges

Generic competition, health care reforms, price pressure, increasing regulatory requirements placed on safety, and health technology assessments of new drugs are some of the trends that are posing challenges in the pharmaceutical R&D environment. We want to ensure sustainable success despite rapidly changing framework conditions. Essential elements of this strategy include focusing on specialist indications with high unmet medical needs, rigorously implementing treatment options adapted to specific patient groups (patient stratification) in order to predict the efficacy of therapies in individual patients, and cooperating with partners. We further expanded our network of alliances in 2010.

In R&D, we continue to build on our expertise in both small molecules and biopharmaceuticals. We are also investigating potentially new compound classes that could lead to innovative therapies. For example, we entered into a partnership with the Belgian company Ablynx to co-discover and co-develop Nanobodies® for use in the area of rheumatology. Nanobodies® are an innovative class of antibody-derived therapeutic proteins that combine the advantages of conventional antibodies with key properties of small molecule drugs.

Funding of innovative projects in multiple sclerosis research

In the field of neurodegenerative diseases, we formed an exclusive partnership with Fast Forward—a subsidiary of the American National Multiple Sclerosis Society. In 2010, we gave grants to four recipients. The funding, which will initially amount to nearly USD 1.5 million, will be used to advance innovative multiple sclerosis research projects in the United States, New Zealand, and the United Kingdom. In addition, we entered into a strategic cooperation with the Institute

Status of our innovative compounds

Therapeutic area	Compound	Indication	Status
Oncology	Erbitux® (cetuximab, monoclonal anti-EGFR antibody) [1]	Adjuvant colorectal cancer [2]	Phase III
		Gastric cancer	Phase III
	Cilengitide (integrin inhibitor)	Glioblastoma (brain tumor)	Phase III
	Stimuvax® (cancer immunotherapy) [3]	Non-small cell lung cancer (NSCLC)	Phase III
	Erbitux®	Breast cancer	Phase II
	Cilengitide	Head and neck cancer (SCCHN)	Phase II
		Non-small cell lung cancer (NSCLC)	Phase II
	Monoclonal anti-integrin antibody (DI17E6)	Colorectal cancer	Phase II
	TLR9 immunomodulator (IMO–2055) [4]	Head and neck cancer (SCCHN)	Phase II
	MEK inhibitor (AS703026/ MSC1936369B)	Solid tumors and hematological diseases	Phase I
	c-Met kinase inhibitors (EMD1214063, EMD1204831) [5]	Solid tumors	Phase I
Neurodegenerative Diseases	Serum-free formulation of Rebif®	Relapsing-remitting forms of multiple sclerosis (MS)	USA: application submitted
		Clinically isolated syndrome (CIS)	Phase III
	Cladribine tablets	Relapsing-remitting forms of MS; Russia and Australia: approved, USA: application submitted [6]	Approved/ applications submitted
		Clinically isolated syndrome (CIS)	Phase III
	Safinamide [7]	Early-stage Parkinson's disease	Phase III
		Mid- to late-stage Parkinson's disease	Phase III
	Immune-tolerizing agent (ATX-MS-1467) [8]	Relapsing-remitting forms of MS	Phase I
	Extended-release formulation of interferon beta-1a [9]	Relapsing-remitting forms of MS	Phase I
Rheumatology	Atacicept (anti-BLyS/anti-APRIL fusion protein) [10]	Systemic lupus erythematosus (SLE)	Phase III
	Fibroblast growth factor 18 [10]	Cartilage injury	Phase II
		Osteoarthritis	Phase I
Endocrinology	Long-acting growth hormone (ARX 201) [11]	Growth hormone deficiency	Phase II

[1] Developed in cooperation with ImClone LLC: Erbitux® is a trademark of ImClone LLC, a wholly owned subsidiary of Eli Lilly & Co.
[2] Sponsored and coordinated by the Fédération Francophone de Cancérologie Digestive (FFCD)
[3] Exclusive worldwide licensing rights acquired from Oncothyreon Inc.
[4] In-licensed from Idera Pharmaceuticals, Inc.
[5] Collaboration with M. D. Anderson Cancer Center
[6] CHMP adopted a final negative opinion on the marketing authorization application in the EU in January 2011
[7] Collaboration with Newron Pharmaceuticals S.p.A.
[8] Collaboration with Apitope Technology (Bristol) Ltd.
[9] Collaboration with Flamel Technologies S.A.
[10] In-licensed from ZymoGenetics, Inc., a wholly owned subsidiary of Bristol-Myers Squibb Company
[11] Collaboration with Ambrx, Inc.

NSCLC: Non-small cell lung cancer
SCCHN: Squamous cell carcinoma of the head and neck
CIS: Clinically isolated syndrome

for Experimental Neurology (INSPE) and the Department of Neurology at the San Raffaele Scientific Institute in Milan, Italy. The aim of the cooperation is to advance clinical research projects in the field of neurodegenerative diseases using new models and technologies.
Merck Serono Ventures is the name of our corporate venture capital fund. In 2010, the fund invested in two highly innovative biotech companies. One of the companies is f-Star from Vienna, Austria, which is engaged in the discovery and development of modified antibodies. The most recent investment was made in Auxogyn of San Francisco. This company is developing a non-invasive tool for early assessment of embryo viability within the scope of in vitro fertilization procedures.
Additionally, internal cooperation with Merck Millipore is creating new prospects. Potential synergies exist in areas such as companion diagnostics, systems biology, new biopharmaceutical drug delivery methods, and in the search for new routes in biopharmaceutical production.

Research and development: Additional potential for Erbitux®

New data on Erbitux® for first-line treatment of metastatic colorectal cancer

Further analysis of the Phase III CRYSTAL trial once again confirmed the therapeutic value of Erbitux®. New data show that patients with KRAS wild-type metastatic colorectal cancer (mCRC) who experienced early tumor shrinkage during first-line Erbitux®-based treatment had an unprecedented overall median survival of 28.3 months. Further Phase III studies are being conducted in gastric cancer (EXPAND) and adjuvant colorectal cancer (PETACC-8).
Initial results of the randomized Phase II trial BALI-1 demonstrated the therapeutic potential of Erbitux® in breast cancer. Treatment with Erbitux® in combination with chemotherapy showed positive results in patients with metastatic triple-negative breast cancer (TNBC). Median progression-free survival in women treated with Erbitux® plus chemotherapy more than doubled. Although tumor response nearly doubled, the primary endpoint of the study, response rate, was not met. TNBC is aggressive, difficult to treat, and associated with high rates of metastasis and relapse.

Stimuvax®: Clinical program resumed, obstacles successfully overcome

In June, Merck resumed the Stimuvax® (BLP25 liposome vaccine) clinical program in patients with non-small cell lung cancer (NSCLC), which includes the Phase III studies START and INSPIRE. The treatment and enrollment of patients has restarted after approval by the local regulatory authorities and ethics committees. This was made possible by a decision by the U.S. Food and Drug Administration (FDA) to partially lift the clinical hold and allow the START trial to resume. The Phase III STRIDE trial in advanced breast cancer was the study that remained on clinical hold by the FDA. Merck Serono decided to close this study.

The clinical hold was put in place by the FDA in March 2010 following a suspected unexpected serious adverse reaction. A patient participating in a Phase II exploratory clinical trial with the cancer immunotherapy in multiple myeloma developed encephalitis. Since 2007, we have been conducting the START trial to evaluate the efficacy and safety of the treatment with Stimuvax® in patients with inoperable stage III non-small cell lung cancer. The decision to initiate this trial was based on the results of a randomized Phase IIb study, in which Stimuvax® showed an increase in overall survival of a subset of patients with locoregional stage IIIb NSCLC from 13.3 months in the control group to 30.6 months in the treatment group. In 2009, we initiated INSPIRE, a Phase III trial in NSCLC in Asia. Should the Phase III trials be successfully completed, this cancer immunotherapy could play an important role in the treatment of lung cancer patients, for whom current therapeutic options are still limited.

Cilengitide trial provides long-term follow-up data in glioblastoma patients

Cilengitide is the first integrin inhibitor in oncology to have entered Phase III clinical development. In the CENTRIC trial, we are studying this compound in glioblastoma (GBM), the most aggressive type of brain tumor. Integrin inhibitors are thought to work by targeting tumor cells and the vascular network required to nourish the tumor and promote cancer cell growth. Long-term follow-up data from a randomized Phase II study of two different cilengitide doses in recurrent glioblastoma were published in 2010. They showed that 37% of patients who received the higher dose of cilengitide (2000 mg) were still alive after one year. The current prognosis of patients with recurrent glioblastoma is poor with median overall survival between four and seven months and one-year survival rates of approximately 20%.

Pipeline: All resources focused on promising projects

Merck Serono remains highly committed to research and development in oncology

Merck Serono remains committed to its discovery and development work in the therapeutic area of oncology. Our aim is to offer patients with high unmet medical needs additional therapeutic options in various indications. An important step toward this aim is the worldwide research and development agreement entered into with Sanofi-Aventis at the end of 2010. This agreement allows the experimental combination of Merck's MEK inhibitor with one of two early compounds of the partner, respectively.

We are currently investigating three compounds in Phase I studies in solid tumors and hematological diseases. In addition, five Phase II studies are underway in breast, head and neck, non-small cell lung as well as colorectal cancer.

Since our pipeline includes numerous compounds with high therapeutic potential, we remain committed to moving forward those projects with the greatest promise of sustainable success. At the same time, we will terminate or divest at an early stage those projects that appear to be less promising. This enables us to ensure that our resources are deployed to benefit patients and to manage the risks for our company. In 2010, we terminated the following four early-stage oncology projects: an aurora-kinase inhibitor and the monoclonal antibody sonepcizumab in Phase I; the immunocytokine tucotuzomab celmoleukin and the monoclonal antibody adecatumumab in Phase II.

Efficacy of Rebif® demonstrated in clinically isolated syndrome

Rebif® significantly delayed conversion to clinically definite MS in patients with CIS

Within our Neurodegenerative Diseases therapeutic area, we are conducting research to discover new therapeutic options for multiple sclerosis (MS) and Parkinson's disease – two indications with high unmet medical needs. In REFLEX, a two-year Phase III study involving more than 500 patients, we investigated whether patients with clinically isolated syndrome (CIS) at risk of developing MS could benefit from treatment with the serum-free formulation of Rebif®. Study participants with this clinical picture have so far experienced a single MS-like episode, such as optical or sensory disturbances, and have characteristic MRI lesions, putting them at high risk of developing clinically definite multiple sclerosis. At this early stage, these patients have not yet been given a clinically definite diagnosis, yet they are at risk of developing MS. The trial, which was completed in October, met its primary endpoint by demonstrating that Rebif® significantly delays conversion to clinically definite 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.

Progress made with the further development of cladribine tablets

With cladribine tablets, the Merck Serono division is developing a drug for the oral, short-course treatment of relapsing-remitting multiple sclerosis. In 2010, we received regulatory approvals in Russia and Australia. Our regulatory application received a negative opinion in the European Union. It is currently under review in the United States (see page 51). The clinical development program for cladribine tablets is designed to evaluate the potential therapeutic effects of cladribine tablets in various stages of the disease. Following the successful completion of the CLARITY study, a two-year extension with around 800 patients is currently underway to provide data on the long-term safety and efficacy of cladribine tablets as a monotherapy in relapsing-remitting MS. The two-year Phase III ORACLE-MS study is investigating cladribine tablets as a monotherapy in patients with clinically isolated syndrome. In November, we completed the recruitment of more than 600 study participants. In the Phase II ONWARD study, we are evaluating the safety and tolerability of adding cladribine tablets to established treatment with interferon beta.

Long-term study completed with safinamide in late-stage Parkinson's disease

Safinamide study misses endpoint, but confirms effect on motor function and safety profile

Together with our partner Newron, we are developing safinamide as an oral adjunctive therapy for patients with various stages of Parkinson's disease, which affects an estimated three million people in industrialized countries. In 2009, we had successfully completed the first Phase III clinical trial of safinamide administered as an add-on therapy to levodopa standard treatment in patients with advanced Parkinson's disease (Study 016). Motor function and the ability to perform daily activities improved significantly in patients treated with safinamide compared to placebo. An 18-month extension study (Study 018) was intended to provide data on the long-term efficacy and safety of safinamide in this indication. We announced the results of this long-term study in November 2010. The primary efficacy endpoint measuring dyskinesia after 24 months of treatment was not met. We therefore reassessed the sales potential of safinamide and recorded an impairment (see page 19). By contrast, the results of the analysis of the main secondary endpoint were consistent with the effect on motor function observed in

Study 016. The data from Study 018 also confirm the safety profile of safinamide. With SETTLE, a further Phase III clinical trial is underway in this indication. In the MOTION study, a Phase III clinical trial, we are evaluating safinamide as an add-on therapy to a dopamine agonist in early Parkinson's disease.

Increasing the success rate after in vitro fertilization

The objective of fertility research and development work at Merck Serono is to help infertile couples at every stage of the reproductive cycle – from follicular development to early pregnancy – to realize their dream of having a child. The innovative drugs and application devices must offer patients maximum ease of use and increase the probability of a pregnancy. In this way, we want to further expand our leading position in the treatment of infertility. Our ongoing research efforts are focused on drugs, technologies and support services that will improve the success rate of in vitro fertilization (IVF) procedures, and thus ultimately increase the take-home baby rate.

Focusing on Rheumatology

In the field of autoimmune and inflammatory diseases, we shifted our focus to rheumatological diseases and consequently renamed this therapeutic area. Our research and development work is centered on molecules that modulate the key pathogenic mechanisms of these diseases. We are developing the recombinant protein atacicept for the treatment of systemic lupus erythematosus (SLE), an inflammatory rheumatological disease. This innovative compound blocks the two immunomodulatory factors APRIL and BLyS. They are important for the survival and the proliferation of lymphocytes that trigger an abnormal immune reaction against the patient's own normal tissues. SLE is a chronic autoimmune disease that mainly affects women and is an area of great unmet medical need. We are currently conducting a Phase II/III clinical trial with atacicept in SLE. Lupus nephritis (LN) is a particularly severe form of SLE involving the kidneys. We are currently adapting the clinical development plan for atacicept in this indication after having discontinued a Phase II / III study in 2008.

Phase II study of FGF 18 started in a new indication, the treatment of knee cartilage defects

Thanks to its novel mechanism of action, fibroblast growth factor 18 (FGF 18) could be the first disease-modifying treatment for osteoarthritis and the repair of cartilage damage following injury. In the laboratory, FGF 18 has been shown to stimulate the regeneration of defective articular cartilage. FGF 18 may support the healing of degenerative joint disease. We successfully completed a Phase I trial of patients with osteoarthritis of the knee joint. A further clinical trial in osteoarthritis is still in progress. We are investigating the efficacy of FGF 18 in the treatment of knee cartilage defects in a Phase II trial that we initiated in 2010.

Research and development on growth disorders and metabolic diseases

The aim of our research and development efforts in endocrinology is to offer patients with growth disorders and metabolic diseases new therapeutic options or improved versions of established products based on our own development work or cooperation with partners. The most recent examples include Egrifta™ (tesamorelin for injection) for the reduction of excess abdominal fat in HIV-infected patients with lipodystrophy, as well as the development of a liquid formulation of Saizen® for injection.