Merck Serono: From living cells to effective therapies

Recent major breakthroughs in the treatment of complex diseases are increasingly due to the use of biopharmaceuticals, in other words active ingredients that have been developed or produced using biotechnology. With the cancer therapy Erbitux® and the multiple sclerosis treatment Rebif®, we have two successful compounds in this drug class in our product portfolio and rank among the leaders in pharmaceutical or "red" biotechnology.
Rebif® is manufactured in Vevey, Switzerland, at the Merck Serono Biotech Center, one of the world’s largest biotech production facilities. This is also where the production of Erbitux® is being prepared. Merck is entering new territory with the start of its own biotechnology production of this drug. The company can draw on the many years of experience of biotech specialists Boehringer Ingelheim Biopharmaceuticals and ImClone Systems Inc. which continue to serve as contract manufacturers of Erbitux®. At the same time, the Merck Serono division is working on numerous new developments in the growth market of biopharmaceuticals that promise therapeutic advances.

With Rebif® and Erbitux®, the division has two products that offer new therapeutic possibilities to thousands of patients around the world. Erbitux® for example: The efficacy and versatility of this targeted cancer therapy has been demonstrated in numerous new studies – not only in the battle against colorectal cancer but also in the treatment of head and neck cancer or lung cancer. Biotechnology research at Merck Serono has also given many patients with multiple sclerosis new prospects for therapy. A new formulation of Rebif®, a drug to treat relapsing forms of multiple sclerosis, has not only improved injection tolerability but also reduced immunogenicity. The European Commission granted approval for the new formulation in August and the market launch began in September 2007. Biopharmaceuticals such as Rebif® and Erbitux® are core components of a broad portfolio that also benefits substantially from the development of chemical molecules using pharmaceutical chemistry. Researchers at Merck Serono have expertise and experience in both technologies and apply them to drug development in a complementary way.

A strong presence in the United States

Measured in terms of sales, the United States is the world’s largest pharmaceutical market. The division, which operates under the name EMD Serono in North America, has a strong footprint in the United States – one of the declared aims of the Serono acquisition.

EMD Serono headquarters in Rockland, MA, south of Boston, houses not only administration and commercial operations but also research and clinical development.

Another research center, along with a pilot plant, is located in Billerica north of Boston. Altogether, more than 850 employees work for EMD Serono to discover, develop and commercialize drugs for use in the therapeutic areas of Neurodegenerative Diseases, Fertility and Endocrinology. Expertise in Oncology as well as Autoimmune and Inflammatory Diseases is also growing. In 2007, the American Cancer Society recognized EMD Serono for its outstanding support in the fight against cancer. With seven recombinant products on the market offering innovative treatments to patients with serious unmet medical needs, EMD Serono is a well-established force in the U.S. biopharmaceutical industry.

New in Japan

Bion®3 made its debut in Japan: The flagship product of the Merck Consumer Health Care division is now also available in the world’s second-largest market for prescription-free, over-the-counter drugs. It is the first product of its kind to combine probiotic cultures with multivitamins and minerals. Bion®3 is marketed by SATO Pharmaceutical, the sixth-largest consumer health care company in Japan. Bion®3 is already marketed in 30 countries around the world.

Cooperation with SATO Pharmaceutical on Bion®3: Merck’s over-the-counter product has been successfully launched in the Japanese market.
Merck Serono is the largest division of Merck. It was established in early 2007 following the acquisition of the former Serono S.A. by Merck and the integration of the business with the former Ethicals division of Merck. Merck Serono focuses on innovative prescription drugs of chemical and biotechnological origin that make important contributions to medical progress.

The business model
Merck Serono focuses on innovative pharmaceuticals. One of the company’s main areas of emphasis is biotechnological products such as monoclonal antibodies and other therapeutic proteins. A strict focus on selected therapeutic areas is an important success factor for Merck Serono in this business – supported by a high level of competence in research and development as well as production and sales. In 2007, Merck Serono generated around 60% of total revenues with six innovative biotechnology products. Products from Merck Serono are marketed in more than 150 countries. Approximately 16,000 employees around the world ensure the division’s global presence.

Key therapeutic areas/products
- Oncology: Erbitux® (metastatic colorectal cancer, head and neck cancer), UFT® (colorectal cancer)
- Neurodegenerative Diseases: Rebif® (multiple sclerosis)
- Fertility: Gonal-f®, Ovitrelle®, Pergoveris™, Luveris®, Crinone®, Cetrotide®
- Endocrinology: Saizen® (growth hormone disorders), Serostim® (HIV-associated wasting)
- CardioMetabolic Care: the Glucophage® family (type 2 diabetes), the Concor® family (cardiovascular diseases), Euthyrox® (thyroid disorders)
- Other therapeutic areas: Raptiva® (psoriasis), Cynokit® (cyanide poisoning) and other products

Market trends and prospects for the future
- According to forecasts by the market research institute IMS Health, the global pharmaceutical market will grow by 5% to 6% in 2008 and reach a volume of around US$ 740 billion.
- Oncology products will continue to achieve the strongest growth rates. According to IMS Health, they will account for nearly 17% of market growth in 2008. Cancer therapies are expected to become the strongest drug group in terms of sales by 2011.
- The market for products prescribed by specialists will continue to grow – by more than 14% to around US$ 300 billion in 2008.
Growth through the Serono acquisition

Merck Serono is the largest division of Merck. In 2007, total revenues were €4,458 million. In order to achieve comparability with 2006, pro forma figures are used in the following section. They compare the figures for 2007 with those of the former Serono Group and the former Ethicals division combined in 2006. Accordingly, organic growth was 7.4%. This is due largely to higher sales of the targeted cancer therapy Erbitux® and Rebif® for the treatment of relapsing forms of multiple sclerosis (MS). Global sales of Rebif® increased in 2007 to €1,218 million, 5.3% more than the amount reported by the former Serono Group in 2006. A new formulation was launched in September in the EU. Sales of Erbitux® also grew steadily. In 2007, they climbed by 40% to €470 million.

With the acquisition of the former Serono Group, the division’s research and development spending nearly doubled to €879 million.

In a pro forma comparison with 2006, the division increased its gross margin by 10% to €3,765 million. The operating result decreased by 52% to €357 million. Among other things, charges of €531 million for the amortization of intangibles in connection with the Serono purchase price allocation should be taken into account. In addition, Merck Serono incurred expenses of €154 million for ongoing integration measures in 2007. Return on sales (ROS) was 8.0%. Nominal free cash flow amounted to €–6,505 million. This primarily reflects the acquisition of Serono. Free cash flow adjusted for acquisitions and disposals was €774 million.

A strong presence in the United States

As a result of the Serono acquisition, sales of the Merck Serono division rose in Europe by 93% to €2,441 million in 2007. In comparison with pro forma sales for 2006, growth was 8.4%. High growth rates were achieved in Spain, Italy and Belgium – also on a pro forma basis. The largest markets were France with sales of €580 million, followed by Germany with €476 million, Italy with €269 million and Spain with €268 million. With sales of €730 million, the new division also has a strong presence in North America due to the acquisition of Serono. Business in Latin America was characterized by growth. Thanks to the acquisition, Merck Serono captured new markets there and posted a 56% increase in sales to €492 million. Pro forma growth was 16%. The division was particularly successful in Brazil, and also generated robust growth in Venezuela and Colombia. Sales in the region Asia, Africa and Australasia rose by 74% as a result of the acquisition. Merck Serono expanded its presence in Japan but remained weak overall.
Therapeutic areas

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Oncology

Breakthrough in important new markets

In the battle against colorectal cancer, the form of cancer with the highest number of new cases in the seven largest markets (United States, Japan, Germany, United Kingdom, France, Italy and Spain), Erbitux® (cetuximab) represents an important treatment option. It is also used as a therapy in the treatment of head and neck cancer. Currently, the cancer drug is approved in 68 countries for combination therapy with irinotecan after irinotecan failure in patients with colorectal cancer and in 61 countries in combination with radiotherapy for the treatment of locally advanced squamous cell carcinoma of the head and neck. Sales of the Oncology business unit totaled € 479 million in 2007. The targeted cancer therapy Erbitux® accounted for a substantial portion of this amount, with sales of the product increasing by 40% to € 470 million. Recent launches in key markets such as China, Russia and Brazil led to increasing sales. In addition, the division has meanwhile filed for marketing approval in Japan – the world’s second-largest pharmaceutical market – for the use of Erbitux® in treating patients with advanced colorectal cancer. Every year, more than 38,000 people die from this form of cancer in Japan. Once approval is granted, Merck Serono will co-market the oncology drug in Japan with ImClone Systems Inc. and Bristol-Myers Squibb.

The division is working to further expand the range of approved indications for Erbitux®. For example, an application to extend the use of Erbitux® to include the first-line treatment of metastatic colorectal cancer was submitted to the European Medicines Agency (EMEA) in September 2007.

Sustained growth in the oncology market

According to forecasts by the market research institute IMS Health, the growth of the oncology market will continue. In the next four years, global sales are expected to more than double. Market researchers expect sales to increase from US$ 35 billion in 2006 to around US$ 80 billion in 2011. In the next four years, an estimated 50 new cancer drugs are to be launched. Market researchers expect monoclonal antibodies such as Erbitux® to achieve average annual growth of 14% and sales of US$ 43 billion by 2012. According to Business Insight, business with innovative cancer therapies is the fastest growing segment of the oncology market and at the same time the growth driver of the entire pharmaceutical industry.
Neurodegenerative Diseases

Sales by this business unit were attributable to Rebif® (interferon beta-1a), the top-selling product of the Merck Serono division. Owing to its favorable benefit-risk profile and proven efficacy, in terms of sales Rebif® is the leading treatment for relapsing forms of multiple sclerosis (MS) outside the United States. Sales of Rebif® increased by 5.3% to €1,218 million in comparison with the 2006 figures of the former Serono Group. Negative currency effects dampened organic growth, which amounted to 9.6%. In the United States, where Rebif® has been approved since 2002, the drug continued to gain market share and generated more than one-third of its sales. In Europe, sales of Rebif® increased thanks to double-digit growth in Spain and the countries of central Europe as well as good performance in Germany.

New formulation of Rebif® now available

The Merck Serono division is investing steadily to further develop and improve its top-selling product Rebif®. In order to further enhance the therapeutic benefit, a new formulation of Rebif® was developed. The data show that the new formulation offers a new three-fold improvement in injection tolerability and reduced immunogenicity compared with historical data for the previous formulation of Rebif® as measured in the EVIDENCE study. At the end of August, the European Commission approved the new formulation of Rebif®. The approval applies to the member states of the European Union (EU), as well as Iceland, Liechtenstein and Norway. The product was approved in Canada in September 2007.
Fertility

Merck Serono is the world’s leading supplier of drugs to treat infertility. The division is the only manufacturer of recombinant versions of all three gonadotropin hormones. Sales by the Fertility business unit declined slightly by 0.8% to €519 million in comparison with sales achieved by the former Serono in 2006. This was due mainly to negative currency effects in the United States, where around 25% of sales were generated. The sale of the marketing rights to Crinone®, a progesterone gel, to Columbia Laboratories, Inc. in the United States at the end of 2006 also lowered sales.

Gaining market share in the United States with Gonal-f®

In a stable and mature market characterized by strong competition, Gonal-f® (folitropin alfa for injection) remains the world’s leading female fertility drug. This recombinant form of the follicle-stimulating hormone (FSH) is prescribed to supplement or to replace natural FSH and is meanwhile approved in more than 100 countries. Sales rose slightly over the previous year to €434 million. Adjusted for currency effects, the increase was 5.7%. After declining in the United States in 2006, sales recovered and market share increased. More than one-half of sales were generated in Europe. Gonal-f® further expanded its share of this important market. In Japan, where Gonal-f® is currently approved to treat male infertility, a clinical development program is underway to expand the indication to include female infertility.

Merck Serono continues to invest in the further development of its products and delivery devices. A new generation of the Gonal-f® pen was launched in Australia and several European countries. The global roll-out of this new product will continue in 2008.

Market launch of Pergoveris™ begins

Merck Serono has developed Pergoveris™ for the stimulation of follicular development in women with severe luteinizing hormone (LH) and follicle stimulating hormone (FSH) deficiency. Pergoveris™ is the first biotech drug based on the combination of both substances in a single subcutaneous injection. Marketing authorization was granted by the European Commission in June and applies to the member states of the European Union (EU), as well as Iceland, Liechtenstein and Norway. The market launch of Pergoveris™ began in the third quarter of 2007.

Sales of Ovidrel®/Ovitrelle® (choriongonadotropin alpha), a recombinant version of the natural pregnancy hormone hCG, continued to grow. In 2007, sales increased by 23% to €28 million. Ovidrel® is used to induce ovulation in women who are not ovulating and remains the leading product in the market for hCG products. It is the first and only recombinant hCG offered in a ready-to-inject, prefilled syringe that is easy to use.
Endocrinology

Merck Serono is also committed to improving the lives of people with a range of endocrine and metabolic disorders. The division’s Endocrinology business unit offers a unique portfolio of specialized therapies along with innovative drug delivery devices. Merck Serono markets recombinant human growth hormone (somatotropin) under the brand name Saizen® 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. In the United States, Serostim® (somatropin) is used to treat patients suffering from HIV-associated wasting, which is estimated to affect up to 8% of HIV-infected individuals.

Sales in the Endocrinology business unit declined slightly by 2.9% to € 218 million as compared with the previous year’s figures of the former Serono. In the United States, where around one-half of sales were generated, the weakness of the U.S. dollar had a negative impact. Sales of Saizen® decreased by 2.1% to € 163 million. Adjusted for currency effects, however, they increased by 2.0%. Sales of Serostim® declined by 4.6% to € 55 million. Excluding currency effects, they rose by 4.4%.

Easypod™ meets with high acceptance

In early 2007, Merck Serono launched Easypod™, an innovative electronic growth hormone injection device. Easypod™ was developed in conjunction with patients and healthcare professionals for once-daily administration of Saizen®. It is the first delivery device of its kind in this therapeutic area and is noted for its improved reliability and convenience. Easypod™ was first launched in Europe, Australia and Latin America, where it has met with high levels of acceptance. In June, Easypod™ won a gold medal in the Medical Design Excellence Awards competition. Easypod™ was also approved by the FDA in October and was launched in the United States in December.

First drug to treat hyperphenylalaninemia

In November 2007, Merck Serono submitted an application to the European Medicines Agency (EMEA) for the marketing authorization of sapropterin (formerly known as Phenoptin™) for the oral treatment of hyperphenylalaninemia (HPA) due to phenylketonuria or tetrahydrobiopterin deficiency. Currently, no drug is approved in Europe to treat these congenital errors in the metabolism of the amino acid phenylalanine. In December 2007, Merck Serono’s partner in the development of sapropterin, BioMarin, received FDA approval of sapropterin for use in the United States. The product is to be marketed there under the brand name Kuvan™.
CardioMetabolic Care & Other Products

Merck Serono has combined its drugs for treating diabetes, cardiovascular diseases and thyroid disorders in the CardioMetabolic Care business unit. In recent years, the understanding of the interrelationships that exist between hypertension, diabetes and thyroid disorders has steadily improved. Merck Serono offers physicians and patients the possibility to more effectively treat an often complex clinical picture by using an integrated therapeutic approach. Sales in the CardioMetabolic Care business unit increased by 7.0% to €829 million, mainly thanks to the strong growth of the Concor® family of beta-blockers and Euthyrox® for thyroid disorders. Merck Serono announced in July that it would transfer the rights to Niaspan® to Abbott, which acquired the original licensee Kos Pharmaceuticals.

Bisoprolol is the leading beta-blocker in Europe
Sales of bisoprolol, the active ingredient of the beta-blocker Concor® product family, rose by 9.0% to €379 million in 2007. The bisoprolol franchise thus remained the top-selling product group in CardioMetabolic Care. Nearly 75% of sales were generated in Europe, where bisoprolol is the leading beta-blocker in terms of sales. The increase in sales of the Concor® family was due mainly to branded products, which developed very well and posted a 10% increase in sales. In particular, Concor®COR for the treatment of chronic heart failure delivered a stellar performance with growth of 20%. Concor® also recorded good growth of 6.5%. This was due primarily to higher sales in regions such as Latin America, Asia, Africa and Australasia, and Europe, where the new Concor® indication to treat heart failure contributed substantially to growth.

Metformin remains the gold standard in diabetes treatment
Around six million patients worldwide in over 100 countries are benefiting from a product from the Merck Serono portfolio of oral diabetes therapies based on metformin. According to the guidelines of the International Diabetes Federation (IDF), the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD), newly diagnosed patients with type 2 diabetes should be treated immediately with metformin (for example Glucophage®). Metformin continues to be the drug of choice for first-line therapy of type 2 diabetes. Despite strong competition from generics, sales of the metformin group rose by 6.6% to €266 million, with Europe accounting for nearly one-half of this amount. While sales of metformin to third parties continued to decline, the branded products from the Glucophage® family generated a respectable 8.7% increase in sales. The more advanced products such as Glucovance® (combination of metformin and glibenclamide) as well as Glucophage® XR (once-daily formulation) performed especially well: Sales of Glucovance® increased by 13% while those of Glucophage® XR more than doubled.

Thyroid hormone Euthyrox® registers 11% increase in sales
Thyroid disorders are among the most prevalent conditions worldwide. According to epidemiological data, more than 200 million people suffer from hypothyroidism, i.e. underactivity of the thyroid gland, and only 20% of them are currently being treated. 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 and Latin America, the division is number one. Sales increased by 8.0% to €136 million in 2007. Nearly
two-thirds of sales were attributable to Europe. Sales of the thyroid hormone Euthyrox®, which is available in more than 70 countries, grew by 11% to €115 million. Around 11 million patients in more than 70 countries are treated with Euthyrox®. At the end of July, three additional dosage strengths of Euthyrox® were launched in Germany.

**Products for other therapeutic areas**

The Women’s Health business is managed by Théramex, a Merck subsidiary in Monaco. With the establishment of the Merck Serono division, Théramex was integrated into the local French country organization. Synergies with the Fertility business unit are being utilized, for example in the co-promotion of Gonal-F®, which began in 2007. The market environment for products to treat menopause complaints remained difficult in 2007. However, in several countries, the market – especially for transdermal estrogens and natural progestins – has stabilized noticeably.

Sales amounted to €110 million. In France, the most important market, market share increased slightly to 30%. In March 2007, Merck Serono announced plans to terminate production in Monaco by April 2009.

Interesting niche products such as the alcohol-dependency treatment Campral® and Cyanokit®, a life-saving treatment for cyanide poisoning, round off the Merck Serono portfolio. Sales of Campral® totaled €36 million in 2007. Cyanokit® (active ingredient: hydroxocobalamine) was approved in Japan in September 2007 and by the European Commission in November 2007 to treat cyanide poisoning.

**Dermatology**

Sales of Raptiva® (efalizumab) increased by 37% to €76 million. Raptiva® is now approved in 64 countries around the world. Used to treat chronic moderate to severe plaque psoriasis, Raptiva® is the only biological psoriasis therapy for which compelling long-term data demonstrate enduring efficacy over a three-year period. It is suitable as a therapy for chronic stable plaque psoriasis, either as induction or as long-term maintenance therapy in responders. Patient quality of life is noticeably improved, also thanks to its ease of use: Raptiva® is administered once weekly via subcutaneous injection and can be self-administered by patients at home.

The use of Raptiva® points to new benefits in treating more difficult forms of psoriasis, for example disease affecting the hands and feet or the scalp.

According to estimates, 2% of the world’s population suffers from psoriasis. Treatment with targeted biotherapeutics could be an option for around 25% of these patients. Merck Serono is therefore working to educate dermatologists on the use of Raptiva® to treat psoriasis and to convince payers to reimburse the costs of this innovative biotech therapy.

Since psoriasis is often considered only a cosmetic problem, public awareness campaigns are necessary. Merck Serono is working together with professional associations and patient organizations in this area. Due to Raptiva’s unique mechanism of action, Merck Serono is considering the submission of this biotherapeutic for approval in other dermatological diseases, such as atopic dermatitis.
Research and development

Research spending by the new Merck Serono division nearly doubled in its first year of operation to €879 million, equivalent to 20% of the division’s total revenues. This percentage is above the global average for research-based pharmaceutical manufacturers. One of the objectives of the integration of the former Serono Group is to deploy R&D resources even more efficiently. Alongside Oncology, Merck Serono focuses on innovative specialist therapies for the treatment of Neurodegenerative Diseases such as multiple sclerosis and Parkinson’s disease, Autoimmune and Inflammatory Diseases and – under the heading Fertility – therapies designed to help infertile couples conceive. Development projects in Endocrinology are also part of the portfolio.

As part of the consolidation process, the division decided to reconsider the further investment in diabetes research and development and is seeking suitable partners to pursue these activities. Continued success in a competitive environment would have required additional measures in terms of research & development and marketing, of a scale similar to the establishment of a new business in this area. The rights to a drug candidate (GRC 8200) to treat type 2 diabetes were returned to Glenmark Pharmaceuticals of India. The required write-off amounted to €28 million.

Instead, Merck Serono is targeting resources toward reinforcing the leadership position already achieved in the division’s therapeutic areas. Realigning research and development opens up opportunities for synergies between the various therapeutic areas. An example is the recombinant fusion protein atacicept, which is being investigated both for oncology indications and for its potential in treating neurodegenerative diseases, autoimmune and inflammatory diseases.

Collaborations expand the portfolio

A multi-year agreement on the discovery, development and marketing of innovative aptamer-based cancer therapies was entered into with Archemix of Cambridge, Massachusetts, USA. Aptamers are a new class of drugs uniting the best properties of small molecules and antibodies. Unlike monoclonal antibodies such as Erbitux®, aptamers are synthesized chemically, which can bring significant cost benefits.

To advance the businesses successfully, Merck Serono is strengthening its partnering and licensing strategy. Examples are the strategic alliance with ZymoGenetics on the expansion of the pipeline for autoimmune and inflammatory diseases, and a cooperation agreement with École Polytechnique Fédérale de Lausanne in the fields of neurology, oncology and nanotechnology.

In addition, Merck entered into a worldwide licensing and collaboration agreement with Idera Pharmaceuticals, Inc. of Cambridge, Massachusetts for the research, development and commercialization of Idera’s Toll-like Receptor 9 (TLR9) agonists for the treatment of cancer. Toll-like Receptors (TLRs) function in human immune cells as the sensors of pathogens. Under the terms of the agreement, Merck has agreed to pay an upfront license fee of US$40 million to Idera.

New options for the treatment of cancer with Erbitux®

The study data on the monoclonal antibody Erbitux® (cetuximab) impressively demonstrate the consistent efficacy and versatility of this targeted cancer therapy. When used in combination with current standard irinotecan-based chemotherapy in the first-line treatment of patients with metastatic colorectal cancer, Erbitux® significantly increased progression-free survival, response and resection rates. The prospects for removing the liver metastases surgically improve considerably – as does the chance of cure. The number of
## Status of our innovative compounds

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<td>ARX 201®</td>
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<td>Fibroblast growth factor 18</td>
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<tr>
<td><strong>Other products</strong></td>
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<td>Type 2 diabetes</td>
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<tr>
<td></td>
<td>FC EPO</td>
<td>Anemia associated with chronic renal failure</td>
<td>Phase I</td>
</tr>
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1 Developed in cooperation with ImClone: Erbitux® is a trademark of ImClone Systems Inc.
2 Exclusive worldwide licensing rights acquired from Oncothyreon Inc.
3 Collaboration with Takeda Pharmaceutical Company Ltd.
4 Inlicensed from Idera Pharmaceuticals Inc.
5 Collaboration with Micromet AG
6 Collaboration with NovImmune S.A.
8 All rights acquired from Santhera Pharmaceuticals AG
9 Collaboration with Newron Pharmaceuticals S.p.A.
10 Collaboration with AstraZeneca UK Limited
11 Collaboration with BioMarin Pharmaceuticals, Inc.
12 Collaboration with Ambrx, Inc.
13 Collaboration with ZymoGenetics Inc.
14 Inlicensed from ZymoGenetics Inc.

EGFR: Epidermal Growth Factor Receptor
EpCAM: Epithelial Cell Adhesion Molecule
EGFR: Epidermal Growth Factor Receptor
SCCHN: Non-small-cell lung cancer
SDC: Small-cell lung cancer
OI/ART: Ovulation Induction / Assisted Reproductive Technology
HARS: HIV-associated Adipose Redistribution Syndrome
patients in whom shrinkage of metastases was large enough to allow a complete resection was three times higher in the Erbitux® group than in the control arm. These encouraging results of the so-called CRYSTAL study underscore the importance of Erbitux® as a new option in the first-line treatment of metastatic colorectal cancer. In addition, a clinical Phase II trial (BALI-1) has been started to study the use of Erbitux® to treat breast cancer. A Phase III trial in gastric cancer (EXPAND) is in preparation.

In the treatment of recurrent and/or metastatic squamous cell carcinoma of the head and neck, a breakthrough was achieved with Erbitux®. A Phase III study (EXTREME) showed that the patients who received Erbitux® in combination with either cisplatin- or carboplatin-based therapy had a significantly longer survival, an almost doubling of the time to tumor progression and a significantly higher response rate compared with patients treated with platinum-based therapy alone. This is the first time in 25 years that a survival benefit has been demonstrated in this group of patients in a randomized Phase III trial.

A Phase III study (FLEX) on the use of Erbitux® combined with vinorelbine plus cisplatin met the primary endpoint of increasing overall survival compared with chemotherapy alone in patients with advanced non-small-cell lung cancer (NSCLC).

Development of further cancer drugs improves prospects for treatment
A novel combination regimen based on the cancer drug UFT® (tegafur-uracil), an oral form of the standard chemotherapy 5-fluorouracil (5-FU) plus leucovorin (LV) administered by infusion, demonstrated a high response rate of 66% in the first-line treatment of advanced metastatic colorectal cancer. This confirmed that UFT® is an effective alternative to 5-FU i.v. in this indication. The further development of the humanized monoclonal antibody matuzumab for the treatment of metastatic colorectal cancer was terminated. A Phase II study on the efficacy of matuzumab in combination with irinotecan failed to meet the predefined endpoint. In addition, Merck Serono returned the rights to develop and market zanolimumab (HuMax-CD4) for the treatment of T-cell lymphoma to Genmab.

Important results were delivered by a randomized Phase II study with Stimuvax® (BLP25 liposome vaccine) – a therapeutic cancer vaccine that Merck Serono is developing to treat non-small-cell lung cancer. Novel therapeutic vaccines can help the body’s immune system to identify tumor cells and to destroy them without attacking healthy cells. Updated survival data in the subgroup of patients with locoregional disease show that in the arm that received the cancer vaccine in combination with the best supportive treatment, after three years more than twice as many patients were still alive compared to the group that received best supportive treatment, but not the cancer vaccine. Based on these positive results, Stimuvax® is now being studied in Phase III trials. The START trial is the first Phase III study to investigate a vaccine in inoperable stage III non-small-cell lung cancer.

With cilengitide, Merck Serono is developing a highly effective drug to treat glioblastoma – a particularly aggressive form of brain tumor. This integrin inhibitor suppresses the new formation of blood vessels (angiogenesis) and cuts the tumor off from the blood supply. In addition, cilengitide acts directly on tumor cells. The clinical activity of cilengitide in newly diagnosed glioblastoma patients was studied in combination therapy with radiotherapy and a chemotherapeutic agent. In nearly 70% of patients, the tumor had not grown further after six months, median progression-free survival was eight months. These results point to the potential of cilengitide to considerably improve the outcome of patients with this aggressive type of brain cancer, without adding major toxicities.
Continuous further development of Rebif®

In the Neurodegenerative Diseases therapeutic area, Merck Serono is conducting research to develop innovative drugs for multiple sclerosis (MS) and Parkinson’s disease, where high medical needs for new therapeutic options exist. The division is investing steadily in the further development of its successful multiple sclerosis product Rebif®. The most recent example was the approval and market launch of a new formulation in Europe. Based on clinical trials, the range of approved indications is to be expanded so that more patients, for example those in the early stages of the disease, can benefit from treatment with Rebif®. REFLEX is among the most important clinical trials on the further development of Rebif® currently being conducted by Merck Serono. REFLEX is a 24-month Phase III registration study of 480 patients that is examining the efficacy of the new formulation of Rebif® in a new indication, namely clinically isolated syndrome. The study participants are patients at risk of developing MS and in whom so far only an MS-like attack has occurred but who have not yet been diagnosed with clinically definite MS. The purpose of the study is to find out whether these patients could benefit from early treatment with Rebif®. Patient recruitment is currently in progress.

The 40-week Phase IIIb IMPROVE study involving 150 MS patients is examining the efficacy of the new formulation of Rebif® versus placebo. The assessment will be based on the measurement via magnetic resonance imaging of active lesions in the brain.

Oral MS treatment would improve therapeutic success

With cladribine tablets, Merck Serono is developing a drug that – once approved – would represent the first therapeutic option for oral treatment of relapsing forms of multiple sclerosis. This is a proprietary oral formulation of a nucleoside analogue which patients would only need to take a few times a year for a period of five days in a single daily dose. It would make treatment considerably more comfortable and improve the prospects for compliance. The safety and efficacy of cladribine tablets as a monotherapy in multiple sclerosis are currently being tested in more than 1,300 patients enrolled in a two-year Phase III study called CLARITY. Patient enrollment was completed in January 2007.

The U.S. Food and Drug Administration has given cladribine tablets fast track designation as a potential monotherapy for patients with relapsing forms of multiple sclerosis. ONWARD, a Phase II study involving 260 MS patients that also started in January, is examining the safety, tolerability and efficacy of cladribine tablets as an add-on to treatment with interferon beta-1a – for example the new formulation of Rebif®.
New mechanism of action in the treatment of Parkinson’s disease
Safinamide, an orally administered alpha-aminoamide derivative with a novel mechanism of action, is currently in late-stage clinical trials. Together with Newron, Merck Serono is developing safinamide as an add-on treatment to existing treatments, such as stable doses of single dopamine agonists or levodopa, for early-stage as well as mid- to late-stage Parkinson’s disease. The results of a six-month Phase III trial with safinamide as an add-on treatment to dopamine agonist therapy in patients with early-stage Parkinson’s disease were presented at the 59th Annual Meeting of the American Academy of Neurology in May. The data showed that the addition of safinamide at a dose of 50 to 100 mg led to an improvement in motor symptoms. In August, Merck Serono announced the results of a twelve-month extension study of this six-month trial. The primary efficacy endpoint, time to intervention, did not reach statistical significance when data from both safinamide dose groups were pooled. However, a post-hoc analysis of the data showed that the addition of safinamide at a dose of 50 to 100 mg once daily to dopamine agonist therapy delays the time to intervention for therapeutic adjustment. The MOTION trial, a Phase III study that was initiated at the end of 2007, will evaluate safinamide in this dose range as an add-on therapy to a dopamine agonist in early Parkinson’s disease.

Merck Serono is developing atacicept together with ZymoGenetics for the treatment of multiple sclerosis. Phase II studies, which will evaluate the anti-inflammatory effect of atacicept in multiple sclerosis, are expected to begin in 2008.

Two substances to treat infertility in development
Research in the therapeutic area of Fertility is intended to help infertile couples to conceive a child, delivering products for every phase of the reproductive cycle from ovulation to early pregnancy. The development pipeline contains many promising new products for initiating ovulation and for improved administration of follicle-stimulating hormone (FSH).

Proteins as factors in autoimmune and inflammatory diseases
Research activities by Merck Serono in the therapeutic area Autoimmune and Inflammatory Diseases focus on proteins that modulate important mechanisms in the development of autoimmune and inflammatory diseases.

Atacicept (formerly known as TACI-Ig) is a soluble fusion protein that neutralizes molecules involved in the development of various autoimmune diseases. Merck Serono is developing atacicept together with ZymoGenetics for the treatment of lupus and rheumatoid arthritis. A Phase II/III clinical trial to study atacicept in lupus nephritis, an autoimmune disease of the connective tissue and blood vessels that affects the kidneys, began in December 2007. In January 2008, Merck Serono received agreement from the U.S. Food and Drug Administration (FDA) regarding a Special Protocol Assessment (SPA) for a Phase II/III trial with atacicept in patients with general systemic lupus erythematosus (SLE).
Fibroblast growth factor 18 (FGF 18) could represent a new treatment option for patients with osteoarthritis, a degenerative disease of the joints. Thanks to its novel mechanism of action, FGF 18 has the potential to become first-in-class in stimulating the regeneration of articular cartilage, thus not only treating the symptoms of the disease.

Development projects on growth disorders and metabolic diseases
A number of development projects on selected growth disorders and metabolic diseases are being pursued in the therapeutic area of Endocrinology. Merck Serono can build upon its long-standing experience in these therapeutic indications.

The furthest advanced project is the development of high-dose recombinant human growth hormone (r-hGH) for the treatment of HIV-associated fat redistribution syndrome, also called HIV-associated adipose redistribution syndrome (HARS). Merck Serono continues discussions with the U.S. FDA concerning the approval of r-hGH for this indication. Serostim® is approved for HIV-associated wasting. A long-acting growth hormone, ARX-201, is being investigated in cooperation with Ambrx, a U.S. biopharmaceutical company, in Phase I/II clinical trials for the treatment of growth hormone deficiency.

In November 2007, Merck Serono submitted an application to the European Medicines Agency (EMA) for the marketing authorization of sapropterin (formerly known as Phenoptin™) for the oral treatment of hyperphenylalaninemia (HPA) due to phenylketonuria or tetrahydrobiopterin deficiency. Sapropterin received Orphan Medicinal Product designation to treat HPA from both the FDA and the EMEA.
Over-the-counter medicines are becoming increasingly important as a way to prevent and treat minor illnesses. The Consumer Health Care division offers consumers high-quality over-the-counter products for preventive health care and self-treatment of minor ailments. Many of these are sold under well-known brand names. Through them, Merck is helping to promote better health and improve quality of life.

The business model
The Consumer Health Care division sees itself as a niche marketer and has been growing stronger than the market for the past five years. The main distribution channels for over-the-counter products are pharmacies, in some countries retail chains, and also mail order. In recent years, the portfolio of brands has been consolidated and targeted to large, international markets where they enjoy a high level of trust.

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®, Diabion® and the world's first probiotic multivitamin brand Bion®3/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®

Market trends and future prospects:
- The market research firm Nicholas Hall expects the consumer health care market to show average annual growth of approximately 4.7% up to 2011.
- Strong impetus is coming from the emerging countries of central and eastern Europe, Latin America as well as east and southeast Asia owing to economic and demographic developments, leading to higher disposable income.
- The general wellness trend and greater self-responsibility in the health care systems of many industrialized countries are increasing the importance of well-known and trusted over-the-counter medicines.

Highlights of 2007:
- Total revenues increase by 5.0%, growing somewhat more strongly than the market
- Strategic brands further strengthened
- Divestment of the St. Gervais brand in France
- Launch of the probiotic multivitamin brand Bion®3 in the Japanese consumer health care market
- Launch of Kidabion® multivitamin syrup in China
- Sustained success of Femibion® with the active ingredient Metafolin® in Europe
Strong brands for consumer health care

Continuing on a growth course
Total revenues in the Consumer Health Care (CHC) division increased by 5.0% to € 420 million in 2007, slightly exceeding total market growth as calculated by the market research firm Nicholas Hall. The division recorded the fifth consecutive year of organic growth ranging between 6% and 8%. According to market researchers at Nicholas Hall, CHC is thus currently the fourth fastest growing business among the world’s top 20 consumer health care companies. The division generated this strong growth mainly as a result of the healthy performance of its strategic brands. Increased marketing activities in 2007 for these products were financed to some extent by the proceeds from the divestment of the non-strategic French brand St. Gervais in the second quarter of 2007.

Gross margin rose by 7.5%. This was due in particular to increased sales of high-margin products such as Femibion® and Diabion®.

The division’s operating result increased by 9.4% to € 60 million in 2007, with strong markets responding to higher spending on marketing and sales.

Free cash flow declined by 20% to € 47 million. This is due on the one hand to higher investments in production facilities and on the other hand to the increase in working capital in order to conduct a higher level of business. Return on sales (ROS) increased by 14.2%.

Growth in Europe – the key market
Europe remains the most important market for the Consumer Health Care division. 70% of total revenues were generated in this region. Sales in Europe increased slightly by 3.0% over the previous year. France and the United Kingdom were the key markets, generating sales of € 90 million and € 77 million respectively, followed by Germany with € 40 million.

The French subsidiary Merck Médication Familiale recorded a 4.6% increase in sales mainly as a result of the continued strong performance of the probiotic multivitamin brand Bion®3, sales of which rose by 73%. This was a solid performance given a generally declining market.
Sales in the United Kingdom fell by 11%. Business continued to be impacted in 2007 by the withdrawal of certain Seven Seas fish oil products, which took place in the first quarter of 2006, due to an impurity found in an ingredient from a third-party supplier.

Sales increased by 14% in Germany. This was driven mainly by the continued success of strategic brands, for example Femibion®. Sales of this vitamin product, targeted to pregnant women, grew by 44%. The cold remedy Nasivin® was also very successful on the German market, with sales up 19%, while Kytta® ointment generated year-on-year sales growth of 13%.

Business developments were strong in Poland. Sales rose by 21% thanks to a 22% increase in sales of Nasivin® and the successful launch of a Kidabion® product line extension. Growth of 9.0% in Belgium was due, among other things, to the increase in Omnibionta® sales. Under this brand name, Merck launched a women’s health product containing Metafolin® (Femibion®) and a probiotic multivitamin product for everyday health protection (Bion®3) in this market.

Sustained success in Latin America
In Latin America, sales increased by 17%. Sales in Venezuela rose sharply by 49% thanks to the success of Cebion® and the fish oil product Maxepa®. In Mexico, the largest market for CHC in the region, the division continued to build on the sustained success of its strategic brands. For example, sales of Diabion®, a product specifically designed for people who either have or are at risk of developing diabetes, increased by 12%.

By contrast, sales in Asia, Africa and Australasia remained stable. Sales in India were strong (+21%). In Indonesia, sales grew slightly by 3.4% despite supply chain problems there, which had a negative impact on business with the vitamin product Sangobion®.

Expanding in Japan and China
The Consumer Health Care division intends to consolidate its strong position in the global consumer health care market by targeting the expansion of its brands in key markets. This will be complemented by investments in new and highly promising markets such as Japan and China. For example, Bion®3, the division’s flagship product has been available in Japan since June 2007. It is marketed there by SATO Pharmaceutical, the sixth leading consumer health care company in Japan. Kidabion® multivitamin syrup, a children’s brand, was launched in China in the fourth quarter of 2007.

CHC will continue to expand the business by strengthening its strategic brands. In addition, innovative concepts are currently being tested in order to extend the reach and relevance of these brands. According to forecasts by Nicholas Hall, the volume of the global consumer health care market will grow to €72 billion by 2011, corresponding to annual growth of around 4.7%. The Consumer Health Care division expects the growth of its total revenues to continue to exceed this sector average.
Strategic brands prosper further

The division’s seven strategic brands recorded total growth of 12% in 2007. These brands include products to strengthen the joints sold under the Seven Seas® brand (Kytta® in Germany), the vitamin products Cebion®, Bion®3 (Multibionta®) and Diabion® for everyday health protection, the women’s and children’s health brands Femibion® and Kidabion® (Haliborange®), as well as the cold remedy Nasivin®.

Sales of Femibion®, the division’s fastest growing brand, climbed 40% in 2007. This performance was attributable to strong growth in Germany (+44%), Belgium (+24%) and Poland (+9.1%) as well as market launches in France and Austria. Femibion® contains the patented substance Metafolin® and provides optimal nutritional supplementation for women planning a child, pregnant women and nursing mothers. Femibion® enjoys a leading position in established markets and gynecologist recommendations play a key role in the success of this brand.

By developing new distribution channels, the division has further improved its access to customers. As a result, consumers in Singapore can now also purchase high-quality nutritional supplements from the British CHC subsidiary Seven Seas directly by mail order.

Thanks to strong exports, the mail order business with Lamberts products – high-quality vitamins, minerals and nutritional supplements – recorded another solid year despite a challenging market in the United Kingdom.
Merck maintains technological leadership in the LCD market

Merck is the world market leader in manufacturing and marketing liquid crystals for liquid crystal displays (LCDs). Products from Merck are used in displays for LCD televisions, notebooks and PC monitors, mobile phones, clocks and watches, measuring instruments, digital cameras, camcorders, navigation systems and many other digital displays. Merck’s innovative strength is evidenced by more than 2,500 patents for liquid crystals, their mixtures and display applications.
Merck’s position in the liquid crystals business remains excellent. Growth in the LCD market, which is being driven by LCD televisions, continues to be dynamic, the business is highly profitable. Merck holds the technological leadership position and, as the market leader, is successfully asserting its position against the competition. The competitive landscape in the LCD market shifted in the course of 2007. Having faced competition in the display technologies known as IPS (in-plane switching) and TN-TFT (twisted nematic/thin film transistor) for some time, Merck is now meeting with competition in VA technology (vertical alignment). Merck was prepared for this and developed strategies based on innovative LCD technologies in order to deal with the new situation and to maintain its leading position. The foundation for this is know-how derived from more than 100 years of liquid crystal production at Merck. This is being complemented by new business opportunities, such as reactive mesogens for optical compensation films. These improve contrast and viewing angle dependency and are used in special foils found in LCD televisions. By leveraging the technological competence existing in the company and cooperating closely with its LC customers, Merck is working to profitably expand the product portfolio. Decades of close local ties to customers offer Merck the best preconditions for maintaining its competitive lead. Third-party recognition also confirms Merck’s leading position. In 2007, the company won various awards for its liquid crystals activities, for example the renowned “Frost & Sullivan European Technology Leadership Award.” In Korea, Merck won the Korean Ministry of Science and Technology Award at the IMID, a major regional venue for the display industry, as well as the Prime Minister’s Korea Investment Award.

Detecting dangerous bacteria

Thanks to its innovative products, Merck has established itself in the food microbiology segment. No other competitor offers such a variety of rapid tests in this user-friendly test format. These compact yet high-performance test plates are able to quickly and reliably detect whether foods contain harmful bacteria or their waste products. Under the brand names Singlepath® and Duopath®, Merck sells a range of microbiological test kits that considerably facilitate quality assurance and quality control for customers – mainly food manufacturers, but also clinical laboratories. This series of practice-relevant products started with tests for E. coli bacteria, verotoxins, Salmonella, Campylobacter and Listeria. In 2007, three new tests were added, such as the one for Legionella – the cause of Legionnaire’s disease, a life-threatening condition that has recently been making headlines again. For laboratory personnel, using the tests could not be easier. This leads to significant time savings: With the Merck Salmonella test, for instance, the results are already available after 48 hours, as opposed to five to seven days with the standard methods.

A sunny future

Solar cells made of conductive plastic distinguish organic photovoltaics (OPV): Not only are they cheaper and lighter, they’re also more pliable and versatile than their silicon predecessors. To promote OPV in Germany, the German Federal Ministry of Education and Research (BMBF) has launched a technology initiative that Merck is participating in. Merck, BASF, Bosch and Schott will invest a total of €300 million; the BMBF is providing €60 million in funding. The goal is to contribute to environmental protection in an era of climate change – based upon Merck’s product range for silicon photovoltaics.

Consumer safety: The microbiological tests Singlepath® and Duopath® can be used to detect contaminants in food quickly, simply and efficiently.

High mobility: Within the scope of a BMBF initiative, Merck is developing flexible solar cells together with cooperation partner Konarka. These cells can replace or recharge batteries for mobile applications.
All over the world, liquid crystals from Merck are found inside most LCD televisions, computer monitors, notebooks, digital cameras, mobile phones, PDAs, MP3 players and many other high-quality displays. Merck is the global market leader in this field and, thanks to continuous investment in research and production, also the technology leader.

The business model
The division’s success is based on close cooperation between interdisciplinary teams and display manufacturers in the Far East. Merck’s future is secured through a broad portfolio of customer-specific LC mixtures, reliable just-in-time deliveries in a highly demanding market with high innovation rates, and a large number of patents. More than 100 researchers based in Germany as well as close to our customers in Japan, Korea and Taiwan are responding to the ever-increasing demand in particular for shorter switching times.

Key product
- licristal® – Liquid crystals and mixtures for super-fast and high-performance displays based on innovative technologies such as VA or IPS (see also page 58).

Additional fields of work
- High-performance OLED (organic light-emitting diode) materials for displays and lighting
- Efficient and environmentally friendly structuring tools for photovoltaic products and displays
- Superior materials for optical films that enhance display image quality
- Printable polymers for flexible displays, solar cells and RFID chips

Market trends and prospects for the future
- The LCD market will continue to grow strongly in the coming years.
- According to forecasts by the market research firm DisplaySearch, the following growth rates are expected for LCD panels, in terms of units sold, for the years 2007 to 2011: 17% for notebooks, 7% for computer monitors and 18% for LCD televisions.
- The major growth driver for computer monitors will be sales in emerging countries, for notebooks the trend toward new flat-panel formats and for LCD televisions diagonal screen sizes exceeding 40 inches as well as extremely flat screens.
- At 100 million units worldwide, sales of LCD televisions are expected to already exceed those of cathode-ray televisions in 2008.
LCD technology prevails

According to studies published in August 2007 by the market research firm iSuppli, LCDs now clearly have the edge over the rival plasma-screen technology. In 2008, around 100 million LCD TVs are expected to be sold worldwide, thus exceeding the volume of conventional cathode-ray televisions sold. According to forecasts by the market research firm DisplaySearch, the volume of the liquid crystal market for all applications is expected to grow by around 20% in 2008.

Double-digit organic growth in total revenues
In 2007, total revenues of the Liquid Crystals division rose by 2.3% to € 916 million – in spite of negative currency effects, which had an even stronger impact than in the previous year. This applies to the U.S. dollar as well as the Japanese yen, South Korean won and Taiwanese dollar. Organic growth was 14%. The division thus successfully asserted its position in an increasingly competitive environment. Again, Merck generated most of its business with major display manufacturers in Asia. In the year-on-year comparison of total revenues, it should be noted that the business with ITO (indium tin oxide) coated glass in Taiwan was divested in December 2006.

Free cash flow increases by 14%
At € 611 million, the division’s gross margin was up 3.3% compared to the previous year. The operating result stagnated at € 487 million. Return on sales was 53.1%. Free cash flow increased by 14% to € 425 million. This high growth rate compared to the previous year was partly attributable to investments in production facilities at the Darmstadt site in 2006, which reduced free cash flow.

<table>
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<tr>
<th>Liquid Crystals</th>
<th>Key figures</th>
<th>2007</th>
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<td>Free cash flow (FCF)</td>
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<td>Free cash flow adjusted for acquisitions and disposals</td>
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<td>ROS in%</td>
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<tr>
<td>2007</td>
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Capturing the Chinese market
In regional terms, sales grew slightly in South Korea – due to currency effects nominally by 1.1%. In Taiwan, sales increased by 1.4%. In Japan – where LC technology originated – Merck achieved growth of 11%. An interesting new market is opening up in China, where the division also expanded business. The total volume of this market, however, is still far below that of the three above-mentioned “home countries” of the LC business.

Research and development further expanded
The division once again increased its investments in research and development, which rose by 18% to € 79 million in 2007. New mixture techniques were developed to secure the technology leadership. In Darmstadt, South Korea and Taiwan, new reliability laboratories were established to test the long-term stability of displays for various applications. In addition, investments were made in expanding production facilities at the LC sites in Germany and Asia. In 2008, a new project will be launched to further expand the liquid crystal production facilities in Darmstadt. This will involve investments of around € 52 million in order to dynamically adapt production capacities to the growing global market and to secure Merck’s leading position.
Focus on VA technology

A main focus of investments in research is to further develop the well-established vertical alignment (VA) technology – with the aim of achieving even faster switching times and sharper contrasts. Although VA LCDs already have extremely fast switching times of less than 8 milliseconds, the goal is to further improve these in order to produce even more brilliant television images. Merck researchers are aiming for switching times of less than three milliseconds. Another sales argument is the viewing angle. Merck’s VA technology enables a viewing angle of more than 170 degrees – without loss of contrast or color shift. Besides VA technology, Merck also has a patent for in-plane switching (IPS) technology, which also enables a screen viewing angle of more than 170 degrees.

OLEDs

Merck OLED Materials GmbH, which comprised Merck’s activities in the OLED materials field, was merged with Merck KGaA on April 1, 2007. The research and business activities were integrated into the Liquid Crystals division. OLEDs (organic light-emitting diodes) are an innovative field of work, which could develop long-term into a promising technology for displays. OLEDs can also be used as light sources for a wide variety of applications.

Trend toward flat, large-format panels

The trend toward ever-larger screens for LCD TVs continued in 2007. Asian manufacturers are investing substantial sums in production facilities for large-format displays, so-called eighth- or even tenth-generation panels. Consumers around the world want ever-larger screens with diagonal sizes of 42 inches and more. At the same time, there is also a noticeable trend toward increasingly flat panels. These open up a range of totally new possibilities, for instance in interior design of homes, where flat televisions can be hung like pictures on the wall. The flattest LCD TVs that are commercially available at present are less than four centimeters thick.
Specialty chemicals from Merck are used throughout the entire pharmaceutical production process from development in the laboratory up to industrial-scale manufacture. They ensure reliable analysis in research and dependable production processes. Expertise in chemistry and customer-centric innovations have made Merck a successful supplier to the pharmaceutical, cosmetics, food, plastics, coatings and printing industries.

The business model
The success of the Performance & Life Science Chemicals division is rooted in a special promise that Heinrich Emanuel Merck gave for the purity of his products back in 1851. This made Merck the global reference standard in meeting the highest quality demands for chemicals used in research and production. Today, Merck is a preferred partner for moving from laboratory scale to industrial production – innovations from the division often help customers to achieve key competitive advantages.

- Merck develops customized solutions for each industrial application and offers customer-centric services extending beyond products, such as special documentation for authorities and online services.
- Merck finds innovative answers to many challenges in environmental protection, product safety and product security by utilizing cutting-edge technologies.

Overview of the three business fields
The business models and key products of each of the three subdivisions are presented starting on page 62.

Market trends and prospects for the future
- The laboratory market is characterized by relatively stable average growth; individual biotechnology segments are showing double-digit growth.
- Statutory regulations on production and product safety, the related process documentation and safety requirements as well as quality controls are increasing.
- Branded goods manufacturers are increasingly moving toward high-quality colors and packaging – a trend that is benefiting the business with effect pigments.
- Ionic liquids offer growth potential, for instance as a replacement for conventional solvents in extraction and separation.

Highlights of 2007
- High sales level grows further, organic growth of 4.7%, return on sales at 11.7%
- New global e-commerce platform developed in 2007 is scheduled for launch in 2008 to open up new distribution channels, especially in the laboratory sector
- Strong growth in Asia and slight growth in Latin America, core European market shows stable growth
Strict focus on customer needs

**Solid business development**
In 2007, total revenues of the Performance & Life Science Chemicals division increased by 1.5% to €1,235 million. Currency effects significantly impacted business in the United States and Asia: Organic growth was 4.7%. Gross margin increased slightly by 0.4% to €615 million. The operating result decreased by 7.0% to €144 million. This was affected by, among other things, the restructuring charges for measures in Switzerland and North America.

Return on sales was 11.7%. Free cash flow remained virtually constant at €132 million. The Performance & Life Science Chemicals division invested €58 million in research and development in 2007.

**Growth potential in Asia and Latin America utilized**
On a regional basis, the Performance & Life Science Chemicals division performed particularly well in Asia and Latin America – with growth of, for example, 29% in India and 18% in Thailand. High double-digit growth rates were achieved in several countries of Latin America such as Venezuela and Colombia, and overall growth amounted to 4.0%. With a share of 45% of sales and stable growth of 3.9%, Europe is still the most important market. Here high single-digit growth was generated, for example, in Germany, Benelux, Italy and Poland, while some countries of southeastern Europe and Spain recorded double-digit growth. Business declined in the United Kingdom.

The Performance & Life Science Chemicals division operates in very different market segments that must be served simultaneously. Merck’s success in this area is founded on a strict focus on customer needs. Application-optimized solutions, modern services and new products stand for quality, value, speed and innovative strength.
Laboratory Business

The business model
The success of the Laboratory Business subdivision is based on a long tradition of offering researchers, teachers and users in industry a broad spectrum of laboratory chemicals in a range of quality grades with certificates of analysis ensuring consistent and comparable results. Today Laboratory Business offers specific solutions and top-rate services for many different laboratory requirements worldwide. It is a single-source supplier serving a global market with its own local companies.

Key products
Customers need full-service solutions that exploit the latest technologies. In order for Merck to find the best answers to their requirements, marketing activities are targeted to customer segments. These include, for example, universities as well as the pharmaceutical, biotechnology, food and beverage manufacturing, and chemical industries. Merck is pursuing targeted approaches so that laboratory work can be performed safely and efficiently. Laboratory Business supplies a global market with important laboratory chemicals:
- Reagents for analysis and other applications, particularly standards for instrumental analysis
- Products for analytical chromatography, microbiology, food and environmental analysis
- A broad range of solvents, salts, acids, alkalis and organic chemicals

Life Science Solutions

The business model
The Life Science Solutions subdivision, which is oriented toward customer needs in a wide variety of sectors, offers products and solutions covering the entire range of the latest technological expertise in chemical and physical processes. The subdivision is responding to increasing regulatory requirements with comprehensive product documentation. Understanding the problems and processes of every aspect of the entire value-added chain of customers makes Life Science Solutions an important partner in the following sectors:
- Pharmaceutical industry and biotechnology, increasingly also the food industry
- Cosmetics industry, where Merck offers not only decorative effect pigments but also functional skin care and protection solutions, for example UV protection

Key products
Life Science Solutions supports the entire life sciences process chain from research to market launch
- Separation and purification materials
- Ionic liquids, which are used to simplify biotechnological processes
- Active ingredients used in pharmaceuticals, cosmetics, sunscreen and skin care products
- Active ingredients for food supplements
- Biological crop-enhancing technologies in crop biotechnology
- Products for technical applications

Pigments

The business model
Merck is one of the most successful suppliers of effect pigments used to differentiate and position packaging and product design in a large number of branded products. In particular, new developments from Merck help to strengthen the brand identity of products. Not only decorative, but also security-relevant aspects, for example brand protection, are important here. First-rate service and extensive application expertise make the Pigments subdivision a strong partner, for example to the automotive industry.

Key products
Merck offers established and innovative effect pigments for the following applications:
- Iriodin® mica-based pearl-luster pigments for plastics, coatings and printing inks
- Weather-resistant pigments for automotive coatings and other outdoor applications
- Pyrisma®: a new line of interference pigments for the coatings industry
- Xirallic® effect pigments with attractive glitter effects
- Colorstream® effect pigments with angle-dependent color travel
- Optically variable, highly transparent and shimmering pigments, e.g. Xirona® and Ronastar®, for cosmetics
- Timiron®, Colorana®: mica-based effect pigments for cosmetics
- Functional pigments, e.g. for laser marking or solar heat reflection
- Candurin®, food and pharmaceutical grade composite pigments.
Laboratory Business

High growth rates in food and water analysis
Total revenues of the Laboratory Business subdivision, which is represented with its own employees in 42 countries worldwide, remained stable in comparison with the previous year. Particularly strong growth was achieved with products for food and water analysis and with products for microbiology. Special mention should be made of the strong increase in the business with manual rapid microbiological tests for detecting harmful and pathogenic microorganisms in foods, such as Salmonella and E. coli bacteria, as well as water quality monitoring tests from the Spectroquant® range.

Good business development with customers in the pharmaceutical as well as food and beverage segments was complemented by growth achieved with customers in the global mining industry. Customers in this segment use tests and reagents from Merck to determine the ore content and purity of mined samples. Sales of test kits and reagents for in-process and final control laboratories to customers in the chemical industry performed well. The business with high-purity solvents developed extremely well in all customer segments.

Innovative rapid tests for water and food
In 2007, Merck launched a series of new products such as Spectroquant® Pharo – new spectrophotometers for food and water testing applications – as well as the instrument-assisted bead-based assays for biomarker detection in pharmaceutical, biotech and academic research. Laboratory Business expanded the range of rapid tests for detection of pathogens, ready-to-use culture media (RTU media) as well as Chromolith® separation columns for chromatography. Innovative packaging solutions were developed for solvents based on eco-friendly plastics as a replacement for glass.

On a regional basis, Laboratory Business performed particularly well in India with high, double-digit sales growth. Double-digit growth was also recorded in central and southeastern Europe.

Life Science Solutions

Substantial growth in business with cosmetic actives
Thanks to the great diversity of products and services in its portfolio, Life Science Solutions achieved solid growth and fulfilled expectations. Total revenues grew organically by 3.7% and nominally, against the background of negative currency effects, by 1.7%.

The business with materials for the pharmaceutical and biopharmaceutical industries showed strong, above-average growth. This market segment includes, for example, pharmaceutical salts and materials for separation and purification in pharmaceutical production, such as the well-established Fractogel™ product range. Production capacities for silica gels are being further expanded. The business with cosmetic actives also posted significant growth. That applies to UV absorbers for sun protection, skin care products such as Ectoin®, as well as Oxynex® ST Liquid, a stabilizer for light-sensitive raw materials used in cosmetic products and perfumes.
The active ingredient dihydroxyacetone (DHA) used in self-tanning agents is the top-selling individual product of the Performance & Life Science Chemicals division. Eusolex® UV Pearls are tiny glass beads in which the UV filter is encapsulated and have been specially developed for active ingredients used in sunscreen formulations.

**Continuing success of Metafolin®**

In the area of nutraceuticals, the success story of Metafolin® – a biologically very active form of folic acid that can be directly used by the body – also continued in 2007. The cooperation with the Consumer Health Care division for global marketing of the products Femibion® and Diabion® is an example of successful, cross-divisional collaboration that benefits customers.

Business with ionic liquids got off to a promising start. Ionic liquids can be used in many areas of chemistry, for instance as a replacement for conventional solvents or for biotechnological processes. This business was strengthened by the acquisition of Solvent Innovation in Cologne, Germany.

The crop biosciences business did not meet expectations. In Life Science Solutions, products for natural crop enhancement free of gene technology were so far focused on soybeans. Following the global trend, new products to significantly expand the range of applications are being tested for corn and other crops in field trials.

On a regional basis, Life Science Solutions registered good sales growth of 5.5% in Asia, Africa and Australasia. In Europe, by far the largest market, growth was 3.9%. In North America, sales declined.

**Pigments**

**Good growth with mica-based pigments**

Due to currency effects, total revenues of the Pigments subdivision increased nominally by 3.4% while organic growth was 7.6%. Pigments achieved substantial success with the strategy of focusing on technologically sophisticated, high-margin products. Growth was generated in all market segments. Core markets of Pigments are the cosmetics, coatings, printing and plastics industries, as well as security applications such as products for brand protection.

Excellent growth was generated by pigments based on the raw material mica, for example the Iriodin® product range for plastics, coatings and printing inks as well as the cosmetics industry. A new product family named Pyrisma™, also based on mica, attracted considerable attention during its debut at the leading European exhibition, the European Coatings Show 2007. These pigments, which were developed in close cooperation with our customers, offer very intense effects and cover an extremely wide color range.
Very strong growth was also achieved with pigments of the Xirallic® range, which are mainly used in automotive paints and were already highly successful in recent years. The range of glass flake pigments was expanded. With their smaller particle size, these pigments offer new application possibilities and new, brilliant color effects. The corresponding pigments for the cosmetics industry are marketed under the brand name Ronastar™. The Miraval® family of products is also based on the same raw material and is used in the industry and technology sector, for example for printing, plastic and coating applications.

**New markets entered**
Since gaining approval from the U.S. Food and Drug Administration (FDA), Candurin® pigments have been sparking considerable interest among customers as special-effect color coatings for foods and pharmaceuticals. The use of Candurin® in pharmaceuticals increases the safety for patients by making it easier for them to distinguish between different tablets and capsules.

With the new products Minatec® 60 CM and Minatec® 51 CM, Merck continued its strategy of continuously launching new developments in both decorative and functional pigments. These new products are used, for example, to prevent the static charging of plastic floor coverings.

**Strong position in Europe and Asia**
On a regional basis, Pigments recorded strong growth, particularly in Europe. In Asia, Pigments benefited from the boom in emerging industrial economies such as China and India. Brand manufacturers in the cosmetics and personal care sector as well as the food industry are attaching more and more importance worldwide to high-quality, special-effect packaging. This is a means of clearly differentiating themselves from the competition at the point of sale, for example on supermarket shelves. Here pigments from Merck can help to positively influence consumer purchasing decisions.
Corporate and Other

The segment Corporate and Other comprises Group administrative costs with respect to holding companies, taxes as well as certain exceptional items not assigned to the individual divisions. As of 2007, the financial result of € –311 million is reported in full in the segment Corporate and Other. Due to high interest expenses, free cash flow of € –406 million was markedly lower than the previous year’s figure of € –234 million [adjusted].

The operating result of the segment Corporate and Other totaled € –72 million in 2007 as compared with € –60 million in 2006.

Generics (Discontinued Operations)

On October 2, 2007, Merck completed the sale of the Generics division to Mylan Inc., Canonsburg, PA (United States) for € 4.9 billion (for details, see page 132 of the Consolidated Financial Statements). The results of this division are therefore reported under “Discontinued Operations”.

Total revenues up until the beginning of October 2007 were € 1,395 million in comparison with € 1,824 million for the full year 2006. The operating result of Generics declined to € 189 million owing to weak business in North America in 2007. Return on sales (ROS) was 13.5%.

Compared with the first nine months of 2006, total revenues of the Generics division in the first nine months of 2007 increased slightly by 3.3% to € 1,387 million. During this period, the division generated approximately one-half of sales in Europe, where good business developments were responsible for a 23% increase in sales to € 672 million. The largest market was France, where sales totaled € 280 million, equivalent to a 26% increase over 2006. In Germany, the Generics division benefited from renewed changes in health care policy framework conditions, which led to a 61% increase in sales to € 86 million. Sales declined in North America by 18% to € 380 million and in the United States by 16% to € 323 million. Sales in Latin America increased by 15% to € 28 million, whereas the region Asia, Africa, Australasia maintained the year-earlier level of sales of € 305 million.

### Corporate and Other | Key figures

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<td>Gross margin</td>
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<td>Free cash flow (FCF)</td>
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<tr>
<td>Free cash flow adjusted for acquisitions and disposals</td>
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<td>–224</td>
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### Generics, Discontinued Operations | Key figures

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<td>Free cash flow adjusted for acquisitions and disposals</td>
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<td>255</td>
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* January 1 to October 2