NOVARTIS AG
Form 6-K
February 09, 2009
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SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 6-K

REPORT OF FOREIGN PRIVATE ISSUER
PURSUANT TO RULE 13a-16 or 15d-16 OF
THE SECURITIES EXCHANGE ACT OF 1934

Report on Form 6-K dated February 9, 2009

(Commission File No. 1-15024)

Novartis AG

(Name of Registrant)

Lichtstrasse 35
4056 Basel
Switzerland

(Address of Principal Executive Offices)

Indicate by check mark whether the registrant files or will file annual reports under cover of Form 20-F or Form 40-F:

Form 20-F: x Form 40-F: o

Indicate by check mark if the registrant is submitting the Form 6-K in paper as permitted by Regulation S-T Rule 101(b)(1):

Yes: o **No**: x

Indicate by check mark if the registrant is submitting the Form 6-K in paper as permitted by Regulation S-T Rule 101(b)(7):

Yes: o **No**: x

Indicate by check mark whether the registrant by furnishing the information contained in this form is also thereby furnishing the information to the Commission pursuant to Rule 12g3-2(b) under the Securities Exchange Act of 1934.

Yes: o **No**: x

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GROUP REVIEW

OUR MISSION

We want to discover, develop and successfully market innovative products to prevent and cure diseases, to ease suffering and to enhance the quality of life.

We also want to provide a shareholder return that reflects outstanding performance and to adequately reward those who invest ideas and work in our company.

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GROUP OVERVIEW

Novartis provides healthcare solutions that address the evolving needs of patients and societies worldwide.

We offer a diversified portfolio to best meet these needs: innovative medicines, cost-saving generic pharmaceuticals, preventive vaccines and diagnostic tools, and consumer health products.

FINANCIAL HIGHLIGHTS

KEY FIGURES CONTINUING OPERATIONS(1) (In USD millions, unless indicated otherwise)	**2008**	**2007**
Net sales	**41 459**	38 072
Operating income(2)	**8 964**	6 781
Return on net sales (%)	**21.6**	17.8
Net income(2)	**8 163**	6 540
Basic earnings per share (USD)(2),(3)	**3.59**	2.81
Research & Development	**7 217**	6 430
As a % of net sales	**17.4**	16.9
Number of associates (FTE)(4)	**96 717**	98 200
Return on average equity (%)	**16.5**	26.4
Free cash flow	**4 301**	3 761

SHARE INFORMATION	**2008**	**2007**
Operating cash flow per share(1),(2),(3) (USD)	**4.31**	3.97
Share price at year-end (CHF)	**52.70**	62.10
ADS price at year-end (USD)	**49.76**	54.31
Dividend(5) (CHF)	**2.00**	1.60
Payout ratio of net income from continuing operations (%)	**53**	51

NET SALES, OPERATING INCOME AND NET INCOME

FROM CONTINUING OPERATIONS(2)

(Index: 2003 = 100%)

2008 NET SALES BY REGION

(% and in USD millions)

(1) Excluding discontinued Consumer Health operations divested during 2007

(2) 2007 results include exceptional pre-tax charges totaling USD 1 034 million (USD 788 million after tax) of USD 590 million for a Corporate environmental provision increase and USD 444 million in restructuring charges for the Forward productivity initiative

(3) 2008 average number of shares outstanding: 2 265.5 million (2007:2 3 17.5 million)

(4) Full-time equivalent positions at year-end

(5) Dividend payment proposed to shareholders for approval at Annual General Meeting in February 2009

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NEWS IN 2008

GROUP	Another year of record results in 2008 from continuing operations, confirming benefits of the strategic healthcare portfolio and led by strong performance of the Pharmaceuticals Division. Novartis positioning itself for continued success and growth in a challenging environment.
	Net sales from continuing operations rise 9% (+5% in local currencies) to USD 41.5 billion. Operating income advances 32% thanks to business expansion and benefits of the Forward productivity initiative launched in 2007 to improve speed, flexibility and productivity. Operating margin improves to 21.6% of net sales from 17.8% in 2007.
PIPELINE	One of the industry s strongest pharmaceutical pipelines providing novel medicines with 152 projects in clinical development (Phase I trials to registration). Many have potential best-in-class status, aiming to advance or create new standards of care. Three 2008 submissions receive accelerated US regulatory review status due to urgent health needs. Meningococcal meningitis vaccines progressing, offering potential for global health benefits.
RESEARCH	Novartis Institutes for BioMedical Research focuses on discovery projects at the intersection of powerful scientific mechanisms and greatest medical needs. Exploratory pipeline advances with 93 new molecular entities. Novartis ranks as having one of the industry s largest biologics pipelines.
PORTFOLIO	Agreement with Nestlé offers rights to acquire majority ownership of Alcon Inc., the world leader in eye care with pharmaceutical, surgical and consumer products. First step completed in July 2008 by purchasing 25% Alcon stake for USD 10.4 billion from Nestlé. Second step provides future rights for Novartis to acquire, and Nestlé to sell, remaining 52% Alcon stake held by Nestlé between January 1, 2010, and July 31, 2011, for up to USD 28 billion.
CORPORATE CITIZENSHIP	Novartis access-to-medicine programs for those in need reach 74 million patients in 2008. Value of contributions: USD 1.26 billion, or 3% of net sales. Dispersable tablet form of antimalaria medicine *Coartem* developed specifically for children. Novartis Vaccines Institute for Global Health opens in Siena, Italy, to develop vaccines for neglected infectious diseases.
DIVIDEND	Proposal for 25% increase in 2008 dividend to CHF 2.00 per share from CHF 1.60 in 2007. Dividend yield rises to 3.8%. Payout ratio represents 53% of net income.
LEADERSHIP	New Group structure as of December 2008 strengthens leadership team. Joerg Reinhardt, Ph.D., takes new role as Chief Operating Officer, reporting to Daniel Vasella, M.D. New division leaders named for Sandoz, Vaccines and Diagnostics, and Consumer Health. Group Head of Quality Assurance and Technical Operations position created. Board of Directors and Dr. Vasella agreed on the terms of a new contract extending his current roles as Chairman and CEO.

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DANIEL VASELLA, M.D.

DEAR SHAREHOLDER

I am pleased that despite the global financial crisis and the early signs of a worldwide recession that marked 2008, Novartis achieved record results both in sales and operating income of its continuing business.

Our diversified healthcare portfolio strategy underpinned our success in a difficult environment. Especially gratifying are the accelerated sales and improved efficiency of our Pharmaceuticals Division. Our newly launched medicines are transforming our portfolio and more than made up for the loss of a number of products in the previous year. Vaccines and Diagnostics continued to show dynamic growth, whereas growth slowed in our generics Division Sandoz. Consumer Health achieved its targets.

On a comparable basis, excluding the sales and operating income of the nutrition businesses we divested in 2007, the Group results were:

- Net sales from continuing operations rose 9% (+5% in local currencies) to USD 41.5 billion.

- Operating income grew 32% to USD 9.0 billion.

- Net income rose 25% to USD 8.2 billion and basic earnings per share increased 28% to USD 3.59.

The performance of the **Pharmaceuticals** Division exceeded the expectations of the market and increased net sales by 5% in local currencies to USD 26.3 billion. This growth was realized not only in new markets, but also in Europe, where key products most notably in Oncology posted double-digit growth rates.

The successful market launches of more than 11 products in the United States, European Union, and around the world contributed USD 2.9 billion to net sales in 2008. In addition to sustained growth of our antihypertensives and cancer medicines, the most successful innovative new products include *Aclasta/ Reclast* (USD 254 million), the only osteoporosis treatment given in a once-yearly dose, and *Lucentis* (USD 886 million), the only treatment proven to preserve and, in some cases, improve the eyesight of patients with age-related macular degeneration.

The **Vaccines and Diagnostics** Division achieved dynamic growth in net sales and continued to make significant investments in the development of the new meningitis vaccines *Menveo* (serogroups A, C, W-135 and Y) and MenB (serogroup B), as well as other innovative vaccines. Millions of infants and young people could benefit from both *Menveo* and MenB, as tens of thousands currently die of meningitis every year, while many survivors suffer from severe long-term consequences.

In the generic pharmaceuticals Division **Sandoz**, net sales grew by 1% in local currencies to USD 7.6 billion. Sandoz presents a mixed picture. Growth was slower than in previous years. Outstanding sales increases in important growth markets such as Russia, Brazil, and Central and Eastern Europe, are in sharp contrast to declining sales in the United States and some West European countries. Delays in new launches and price erosion are the main reasons for stagnation in these markets. In Germany, Sandoz is the leading generics company and is gaining further market share. As a result of price cuts, however, the market has contracted and competition has become tougher. On the positive side, Sandoz is in a pole position in biosimilars. In the future, it will be crucial

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that we are the first to launch new products and that Sandoz further extends its leading position in biosimilars.

With increased net sales of 4% in local currencies to USD 5.8 billion, the **Consumer Health Division** met its targets and also gained market share in several segments. The most important driver of growth was CIBA Vision, which under new leadership launched a number of new products and resolved its prior supply and delivery challenges. Animal Health also achieved good results, especially in the companion-animal business, but its farm-animal business was negatively affected by the recession. OTC is expanding rapidly in the emerging markets and in Japan. But, like other manufacturers of OTC brands, the business struggled with the economic downturn in the United States.

We achieved our strong overall performance in 2008 against a background that remains difficult, despite fundamentally robust prospects for growth. Compared to many competitors, however, our strategy of focused diversification in healthcare puts us in a better position to capitalize on growth opportunities in a number of markets and, at the same time, to spread our risks. It is interesting to note that our portfolio strategy now enjoys broad support and that a growing number of major pharmaceutical companies are also investing in generic pharmaceuticals.

It is gradually becoming clear that, like all entrenched dogmas, the usual comparison of companies that are pure plays with so-called conglomerates fails to present the real strengths and weaknesses. It is obvious that a strategy of unfocused diversification is bad, because you are in unfamiliar territory up against competitors with a much stronger concentration on core competencies. However, I believe that Novartis has pursued a different path, one of focused diversification that also allows us to develop our core business, which both differentiates us and adds value.

Thanks to our strategy, in 2008, Novartis stayed on course and completed several targeted acquisitions and strategic investments that both strengthened the portfolio and enhanced our internal growth drivers. For example, Novartis acquired a 25% stake in Alcon, the world leader in eye care. This transaction is part of an agreement that offers Novartis the opportunity to acquire a majority holding in Alcon.

With the purchase of Protez Pharmaceuticals, a privately owned US biotechnology company, Novartis acquired the rights to PTZ601 in Europe and the United States. This very promising antibiotic in Phase II development has the potential to treat life-threatening nosocomial infections.

Novartis also acquired Speedel Holding AG, a company in which we already had a minority stake. This essentially allowed us to acquire all the rights to *Tekturna/Rasilez*.

Despite cost pressures, the demand for medicines and treatments will nevertheless continue to rise. This demand will be driven by the following factors:

• **An aging world population with an increased need for medical care.** This continuing trend is important because, after age 55, there is an exponential rise in chronic disorders such as degenerative diseases of the joints, the cardiovascular system, and the central nervous system. The risk of cancer also increases with age. The impact of disease also heightens with advancing age due to co-morbidity. For example, over 80% of 80-year-olds suffer from at least one disease, and more than 60% suffer from two or more diseases.

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- **Unhealthy lifestyles and environmental pollution increase the frequency of chronic diseases.** Changes in eating habits and lifestyles that include very little exercise, as well as pollution especially air pollution are taking their toll in obesity, chronic cardiovascular diseases, diabetes, cancer and lung diseases.

- **Economic growth in emerging markets with improved access to medicines.** Economic growth that despite the financial crisis remains relatively robust in countries with large populations such as China, creates disproportionately high growth in demand for better healthcare in these countries.

- **Scientific and technological advances** allow new approaches in drug research that create the foundation for innovative medicines for hitherto untreatable diseases.

The cost increases associated with the growing demand for healthcare services, diagnostics and medicines lead to political activities aimed at reducing expenditures on medicines, via price reductions and generic substitution. Unfortunately, these efforts go even further and also encompass attempts to weaken patents and intellectual property. This increases the risk that long-term investment in research and development will decline. Effective medicines ultimately offer the most cost-efficient treatment for a patient and for lowering costs for the healthcare system. The weakening of protection for innovation with potential curtailment of research and development, will not lower costs in the long run, but will instead lead to massive increases in costs not to mention the human suffering. In short, the best way of reducing the long-term costs of healthcare is to provide incentives for sustainable investment in successful research and development. Without better prevention and innovative medicines, the costs of treating patients with cardiovascular diseases, cancer, diabetes or dementia not to mention other diseases will skyrocket.

The past year was marked by a severe financial crisis and recession. The recession will likely intensify over the current year and leave deep scars on the economy and the sociopolitical climate. The healthcare sector will not be spared, although it is considered a defensive sector and generally much less affected by economic factors than other industries. The pressure on prices will continue to increase because public funding (and in many countries also private budgets) will be constrained by dramatic levels of debt. This year we expect new policies from the incoming US administration, which wants not only to provide all its citizens access to medical care, but also to stem the rising costs of its healthcare system.

To provide cost-effective healthcare, all systems around the world must achieve three goals: quality assurance in diagnosis and treatment, access to all essential medical services and medicines, and financial sustainability. This requires greater transparency and comparability of treatment results with standardized treatment methods, measurement, databases and information technology systems. There has been little meaningful progress to date in these areas not only because systemic analysis and planning have been lacking, but also because politicians have been focused on short-term success. Moreover, there are many groups who are resistant to any fundamental change in healthcare.

Criticism of markets and corporations will likely increase over the next few years, extending among some, to a questioning of the principles of a free-market economy and capitalism. One thing is certain: The state has positioned itself as the only actor capable of engendering trust amidst the current financial crisis. There is a risk of a growing belief in state intervention, and the temptation to extend the capacity and scope of state responsibility in naive and dangerous ways. This is also true in the field of corporate governance. We have witnessed a shift in power from management to the board of directors, and then from the board of directors to shareholder activists. Lawmakers are increasingly influenced by activists who seek to restrict the actions of corporations, their owners and their representatives. I question whether these pressures reduce risks. They do, however, curtail the freedom of companies a disturbing development even if it stems from the best of intentions.

Optimism for the future and faith in progress will erode if freedom and risk are increasingly associated with chaos and failure. In a fast-moving modern world, some believe that restrictions promise order and therefore engender a feeling of security and protection. This is a fallacy. The erection of walls either intellectual or economic ones only further heightens the crisis. It is more important than ever before, that we endorse open markets, multilateralism and embrace a point of view that sees the opportunities of globalization and not only the threats. In a society in which control and order are valued most highly, a mentality of entitlement, coupled with hostility to reform and innovation will triumph.

Society has every reason to believe in the power of innovation. Over the last 40 years, we have witnessed a significant reduction in mortality due to numerous diseases. Deaths resulting from rheumatic fever and rheumatic heart disease have fallen by more than 60%, while deaths from hypertensive and ischemic heart disease have fallen by more than 40%. There has been impressive progress in reducing the number of patients who die from cancer. The results

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are especially striking in children, as over the last 25 years, mortality has more than halved. Moreover, medicines are responsible for 40% of the increased life expectancy and have helped to reduce chronic disability in seniors by 25% over the last 25 years.

Our **pipeline** continues to make encouraging progress, and this success not only gives me cause for optimism, but is also in line with our corporate social mission. In research, Mark Fishman and his team have discovered many new biologic targets and 93 highly promising new molecular entities. For the first time, promising new compounds for the treatment of motor disturbances associated with brain disease, cancers and bone metastases that are difficult to treat, metabolic disorders, and juvenile rheumatoid arthritis have entered clinical trials. Our scientists are currently engaged in 152 projects in various stages of clinical development. These include our new cancer medicine *Afinitor* (everolimus, formerly RAD001). In patients with advanced kidney cancer who did not respond to any of the standard treatments, this product has shown a 70% decrease in the risk of progression. Further indications are under investigation. Also highly promising are the clinical results reported with FTY720, a tablet for the treatment of multiple sclerosis, as well as the results of QAB149 for the treatment of chronic obstructive pulmonary disease.

In 2008, Novartis was the only pharmaceutical company with three medicines under priority review by the US Food and Drug Administration. In addition to *Afinitor*, these included *Gleevec/Glivec* as adjuvant therapy in gastrointestinal stromal tumors (GIST) and *Coartem* for malaria. In December 2008, the FDA approved *Gleevec/Glivec* for this additional indication. In this context, it is important to note that, for some time, US authorities have followed much more rigorous safety requirements, and it is impossible to predict timing or chances for regulatory approvals of new medicines.

Payor influence over medical decisions in Europe and in the United States has been growing. These customers place greater emphasis on evidence that new treatments offer better results and improved cost/ benefit ratios.

As investments in research and development increase and pressure on drug prices becomes more intense, efficient cost management becomes even more important. To achieve our objectives, we need to further streamline our organization and processes so that decisions can be made more quickly and be more systematically implemented.

In the context of the economic uncertainty and volatility of the global market, it is increasingly clear that we took the right step in launching the Forward initative. We exceeded our own savings targets and, in some cases, we also fostered renewed growth. Our aim is to save USD 1.6 billion by 2010. The initiative also enabled us to simplify our organizational structure and accelerate decision-making processes.

Our business success allows us to continue our **corporate social responsibility** activities. With our unique malaria and leprosy programs, we have provided more than 200 million treatments since 2001 and helped to save the lives of more than 500 000 people.

Last year, we also launched the Novartis Vaccines Institute for Global Health (NVGH), a nonprofit research institute in Siena, Italy, dedicated to the development of vaccines for patients in developing countries.

Our commitment to patients is an integral part of our strategy. The same is true of the ethical principles anchored in the Novartis corporate culture. I am most pleased that The Dow Jones Sustainability Index recognized Novartis as healthcare super sector leader in 2008. The indispensibility of these principles has become even more clear over the last few months as we are all burdened by the irresponsibility of certain actors in the financial sector which has deeply harmed the global economy.

The promotion of talented leaders to key management positions is critical to the **future success of the company.** In November, Joerg Reinhardt assumed the new position of Group Chief Operating Officer reporting to me. Joerg Reinhardt is succeeded as Head of Vaccines and Diagnostics by Andrin Oswald, previously CEO of Speedel and Global Head of Pharmaceutical Development Franchises in Pharmaceutical Development. The Board also appointed George Gunn Head of the Consumer Health Division, in addition to his role as Head of Animal Health. He replaces Thomas Ebeling, who decided to pursue his career outside Novartis. During his tenure with Novartis, Thomas Ebeling made outstanding contributions, and I would like to take this opportunity to express my sincere thanks to him. Andreas Rummelt assumed the newly created position of Group Head of Quality Assurance and Technical Operations and remains a member of the Novartis Executive Committee. Jeff George, formerly Head of Emerging Markets in the Pharmaceuticals Division, is the new Head of Sandoz. David Epstein now heads a new unit focused on the development of innovative molecular diagnostics in addition to his responsibility as Head of Oncology.

William George, member of the Board of Directors, has decided not to stand for reelection at the next Annual General Meeting. At this meeting, the Board of Directors will propose that Dr. William Brody be elected to the Board of Directors. Dr. Brody served until recently as president of Johns Hopkins University and is now president of the Salk Institute.

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As a shareholder, you are naturally interested in the further development of our company. Our ten-year total shareholder return, including dividends, which we have continuously increased, and business spin offs, surpasses that of the global market, the pharmaceutical industry index, and the performance of key competitors. The tumultuous stock market of 2008 also made it clear that we are seen as a defensive stock delivering strong performance. This view has been supported by the fact that we managed to weather the financial crisis and remain intact both operationally and in our investment activities thanks to our conservative strategy focused on sustainability.

In 2009 we anticipate another year of record results in net sales and earnings. All the elements for success are in place: products, resources, creative thinking, a determination to succeed through an even greater focus on our customers, as well as a competent management team that is distinguished by ambition and integrity.

I expect Joe Jimenez and the management team of the Pharmaceuticals Division to take advantage of the strong performance in the years ahead by investing in research and development, growth products and strategic markets. This will help to ensure that the Pharmaceuticals Division is prepared for the challenging period after 2012, when we can expect generic competition for our top-selling product *Diovan*. Our focused diversification strategy will also provide us with further growth opportunities beyond pharmaceuticals.

There are many changes taking place at the moment, but one thing remains constant: Patients need the best and most cost-effective medicines. I am certain that if we never lose sight of this fundamental imperative, we will succeed in meeting the major challenges of the future.

I would like to thank all our associates for their excellent work, their entrepreneurial mindset and their contributions to the achievement of our objectives. I am especially gratified that our associates understand the need to reorient our organization to a difficult and challenging environment.

Finally I would like to thank you, our shareholders, for the trust you place in our company. I am pleased to be able to propose an increase in the dividend to CHF 2.00 (+25%) at the next Annual General Meeting.

Sincerely,

/s/ Daniel Vasella
Daniel Vasella, M.D.
Chairman and Chief Executive Officer

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HEALTHCARE PORTFOLIO

Innovation is flourishing, bringing new effective treatments to patients. There are significant challenges, however, and the healthcare environment is undergoing unprecedented change.

The world s population is aging. Better healthcare treatments are needed, also prompting payors to manage costs aggressively. Advancing science and technology are enabling new drug discovery while increasing the cost of innovation. Economic growth in emerging countries is providing better healthcare access, but the poorest still lack basic medicines. Changing lifestyles are leading to higher prevalence of chronic and degenerative diseases.

Our strategy is to provide healthcare solutions that address the evolving needs of patients and societies worldwide.

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HEALTHCARE PORTFOLIO OVERVIEW

We believe our portfolio best meets the varied and often complex needs of patients and societies. Novartis is positioned to lead in innovation, partner with others and offer solutions to patients across a broad healthcare spectrum. In addition, a diverse portfolio reduces financial risk, bringing greater value to those who invest in our company.

Novartis has been transformed since its creation in 1996 when only 45% of net sales came from healthcare into a leader focused on fast-growing areas of healthcare.

Novartis is currently organized into four divisions:

- Pharmaceuticals: Innovative patent-protected medicines
- Vaccines and Diagnostics: Human vaccines and diagnostic tools to protect against life-threatening diseases
- Sandoz: Generic pharmaceuticals that replace branded medicines after patent expiry and free up funds for innovative medicines
- Consumer Health: Readily available products that enable healthy lifestyle choices: OTC (Over-the-Counter), Animal Health and CIBA Vision.

NOVARTIS IS NOW A LEADING HEALTHCARE COMPANY

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NET SALES BY DIVISION (1)
(Index: 2003 = 100%, Vaccines and Diagnostics since 2006 acquisition)

OPERATING INCOME BY DIVISION (1)
(Index: 2003 = 100%, Vaccines and Diagnostics since 2006 acquisition)

2008 NET SALES BY DIVISION
(% and in USD millions)

2008 OPERATING INCOME BY DIVISION
(% and in USD millions)

2008 NET SALES BY REGION

(% and in USD millions)

(1) Excluding discontinued Consumer Health operations divested during 2007

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EMERGING MARKETS: BUILDING FROM STRENGTH TO CAPTURE GROWTH

Emerging markets represent a major growth opportunity for Novartis. Growth in healthcare expenditure, fueled by enormous unmet medical need, is outpacing economic expansion in China, India, Russia and Brazil. The dynamic performance of Novartis in emerging countries during 2008 reflects solid positions built over decades as well as increased investments targeting a wide range of scientific and commercial activities. Acknowledging the diversity among emerging countries, Novartis is assessing a number of strategic models tailored to local conditions and the Group s position in each country.

In 2008, emerging countries delivered robust double-digit net sales growth for Novartis. The strategic importance of these markets will increase further in coming years amid slowing growth in the United States and Western Europe.

Though performance of these emerging markets may fluctuate, their potential for Novartis reflects solid positions built over decades, as well as increased investments targeting a wide range of scientific and commercial activities.

One example is the biomedical research and development center under construction in Shanghai, China, a significant investment focusing on infectious causes of cancer that are endemic in Asia. We re looking for great scientists, and China has an incredible pool of talent. We would ignore it at our peril, says Mark Fishman, M.D., President of the Novartis Institutes for BioMedical Research and member of the Executive Committee of Novartis.

Another example is Brazil, where Novartis is the only global pharmaceutical company with local production of active pharmaceutical ingredients. Stimulating chemical production is a key policy goal of the Brazilian government. During the past three years, Novartis has invested to expand capacity at a manufacturing site in Resende, Brazil, creating 200 new jobs. Resende exports an important chemical precursor used in the manufacture of *Diovan*, the world s best-selling branded antihypertensive medicine. Expansion of the Resende site reinforces the position of Novartis as Brazil s largest international pharmaceutical company.

Sandoz, the generic pharmaceuticals Division of Novartis, is also the leading generics company in Central and Eastern Europe and continues to outgrow competitors in the region. You see burgeoning economic growth in these countries and expenditure on healthcare is rising even faster, says Andreas Rummelt, Ph.D., Group Head of Quality Assurance and Technical Operations, member of the Executive Committee of Novartis and Head of Sandoz until December 1, 2008. And when people spend on medicines, they go for generics first.

In Turkey, Novartis is also the largest international pharmaceutical company and number two overall. Novartis has been active in Turkey for more than 50 years, and today four local manufacturing sites supply Novartis medicines to patients in more than 80 other countries around the world.

Turkey is a young country, with more than half the population under age 25, but the demographics will shift rapidly in coming years. Our aging population, the increasing incidence of chronic diseases, and low per- capita drug consumption will be the most important trends in the Turkish market over the next five years, says Guldem Berkman, Country President and Head of the Country Pharmaceuticals Organization. She adds:

You see a clear growth path for the future.

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Emerging markets vary widely. Recognizing that diversity, Novartis is assessing a number of strategic models tailored to local conditions and requirements to accelerate growth.

These large emerging growth markets are where the US was 20 years ago, and it s a huge opportunity for us over the next decade, says Joseph Jimenez, Head of the Pharmaceuticals Division and member of the Executive Committee of Novartis. The division has created an Emerging Growth Markets (EGM) organization focusing on the biggest emerging countries. You are going to see us shift our center of gravity toward some of the faster-growing markets, significantly expand the size of our sales forces and step up clinical development activities in an effort to take businesses already growing rapidly to even higher levels.

At the same time, a unique cross- divisional model is being tested in a number of pilot markets. And in India, Novartis is attempting to build a business catering to the needs of millions of low-income people living in rural villages.

PHARMACEUTICALS: A HEAD START

In major emerging markets the Pharmaceuticals Division is stepping up investments in anticipation of sustained double-digit growth during the next decade. These markets represent the biggest opportunity that currently exists in the global pharmaceutical market, says Jesus Acebillo, M.D., Head of Region Emerging Growth Markets at Novartis. Projected growth for the EGM markets is about 12% per annum, more than double the anticipated growth in the rest of the world. By 2020, sales of prescription medicines in EGM markets are expected to reach USD 400 billion, or 20% of global prescription drug sales, up from an 8% share today.

Growth of healthcare investments has outpaced the rapid economic expansion in China, India, Russia and Brazil in recent years. That momentum is likely to be sustained, despite the current global economic downturn, because of the yet-uncovered medical need of the population in these countries.

Large and growing middle classes are driving healthcare spending. Because health insurance coverage remains inadequate in most major emerging markets, patients pay an important share of healthcare costs out of their own pockets.

For all the recent improvement in economic conditions, emerging countries still face enormous unmet medical need. According to Dr. Acebillo, the frequency of cancer is expected to climb 50% in EGM markets in the next decade due to increased life expectancy. Moreover, about half of all smokers and 75% of people with high blood pressure worldwide live in EGM countries. Obesity and diabetes are growing public health challenges.

Virtually all major pharmaceutical companies today are racing to expand in the biggest emerging markets. Novartis got a head start by establishing the EGM regional organization in 2004. We accumulated a lot of valuable experience during those four years, Dr. Acebillo says.

Growth prospects are galvanized by the large portfolio of new medicines from Novartis being rolled out worldwide. We have doubled sales in the EGM countries since 2004, and we hope to double sales yet again by 2012, Dr. Acebillo says.

Because emerging markets are prone to volatility and instability, Novartis is stressing risk-management skills in development of senior executives across the EGM region. The ability to minimize risk in management of working capital and investments will be key to success, Dr. Acebillo says, together with flexible strategies that can be modified in response to abrupt changes in the operating environment.

Perhaps the biggest hurdle will be recruiting and retaining the thousands of new associates needed to meet the challenges of continued growth in these markets.

Dr. Acebillo expects a fierce battle for talent, which already is in short supply in priority EGM countries. There is a limited number of people with international experience plus language and other skills needed to work in global companies, he says.

Turkey offers a success story in talent management in an era of declining employee loyalty and active recruiting by rival companies. According to Ms. Berkman, Novartis Turkey s country president, employee turnover is about 7% per year, but only 1% among associates rated high-potential. It is essential for Novartis to remain competitive in terms of compensation and benefits, but surveys at the Turkish unit also give management high marks for empowerment and fostering a sense of responsibility for their work among associates.

As a woman heading a large company in Turkey, Ms. Berkman personifies the increasing diversity among senior Novartis managers. After graduating with a degree in chemical engineering from a prestigious Turkish university, she spent the early years of her career with international companies in the fast-moving consumer goods industry, then joined Novartis in 2001 and held positions of increasing responsibility in Marketing and Sales. She was appointed Head of Novartis operations in Turkey at the beginning of 2008.

When I started at Novartis, it was a bit challenging because most people had spent their entire careers in the pharmaceutical industry, Ms. Berkman says. But that has changed, and today it s recognized that people from different industries bring new skills that are a positive contribution to the company.

OTC: NUMBER ONE IN RUSSIA

Over the past decade, Novartis has assembled Russia s leading over-the-counter (OTC) or self-medication business, driven

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largely by growth of the OTC Business Unit but also complemented by sales of OTC products by Sandoz. It is a success story Novartis aims to emulate in other emerging markets.

Back in 1999, prospects seemed bleak. We had a very small business, 10 employees and a few brands nothing to speak of, really, recalls Dionysios Bouzos, longtime general manager of the Russian OTC unit and today Region Head Russia/India/China for the business. It was a very difficult time, following a massive banking and economic crisis in Russia the previous year. No one really knew what the future of Russia would be.

Today Russia is the fourth-largest OTC market for Novartis, measured by sales. Success factors include a tenacious local management team, strong brands and an agile response to rapidly changing market conditions. In addition, a comprehensive information system tracks sales and consumption for more than 25 000 pharmacies across Russia, untangling the underlying trends in this highly complex market.

So armed, Mr. Bouzos was able to increase geographic coverage across the huge, fragmented country while keeping costs under tight control. You marry people, the information system and analytical tools to understand the business and make the right decisions, he says.

Some of the early recruits who started as sales representatives calling on pharmacies have advanced to positions as regional managers, responsible for several territories and multi-million-dollar budgets. I don t think anyone would have imagined back then that we would come so far so fast, Mr. Bouzos says.

Novartis global brands have leading positions in the Russian market across most of OTC s strategic categories: antifungals with *Lamisil*, cough and cold with *Theraflu,* decongestants with *Otrivin* and skin irritation with *Fenistil.* In addition, *Voltaren* is Russia s number two brand in topical pain.

Russia has significance beyond its number four rank in our OTC portfolio. It provides a model for what we can and must do in other high-potential emerging markets, for example China and India, says Larry Allgaier, Global Head of the OTC Business Unit. It is a place where innovation, sales and marketing have come together to bring our goal of being the fastest-growing and most innovative OTC company to life.

The estimated 40 products poised for launch in Russia within the next three years include premium products from the global OTC pipeline as well as rebranding opportunities. A lot of secondary and tertiary Novartis brands are being given new life under global brand umbrellas, and Russia is one of the leaders in that process, Mr. Bouzos says. Sore-throat products, previously missing from the Novartis portfolio in Russia, are being piloted under the *Theraflu* brand. Other examples include *Sinecod* cough syrup, *Pulmex* chest rub and *Vibrocil*, a topical nasal decongestant available in multiple formulations.

In addition, affordable mid-tier brands are a key tool to improve access to high- quality OTC products for a wider number of consumers in Russia. The power of Novartis brands reflects a higher expectation of quality in markets in which substandard copies and counterfeits are widespread.

Another fundamental change during the past decade is the rapid emergence of sophisticated, knowledgeable and discerning Russian consumers, very engaged with their health, he adds. We have to ensure that we continue to provide the kind of innovative products such demanding customers are looking for. In Russia, innovation is an imperative, not a luxury.

For all of the success so far, Mr. Bouzos cautions that Novartis must remain enormously agile to respond to emerging market trends. Changes in Russia are happening so quickly that you don t have the luxury of waiting to see the final result. There is a

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lot of scramble, he sighs. But at the same time it creates enormous opportunities to win if you are quick, resourceful and know the market.

GEM: THE BROAD HEALTHCARE MESSAGE

Group Emerging Markets (GEM), a cross- divisional organization that aims to achieve critical mass and accelerate growth in smaller emerging markets, is operating in nine pilot countries.

In these markets, the country head oversees local Novartis business as a whole, drawing on the uniquely broad portfolio of healthcare businesses to address the needs of patients, physicians, pharmacists and governments. The aim is to boost sales by capturing synergies between divisions and business units, and ensuring a joint approach to key stakeholders and customers all while pooling shared services in infrastructure and back-office areas such as finance and human resources.

Criteria used to select GEM countries included long-term potential of a market and fragmented local operations that prevented Novartis from taking full advantage of opportunities for growth. There was also a desire to test the GEM concept in multiple geographical regions.

We observed that we have markets so small that they fall below the radar screen of some divisions, says Daniel Vasella, M.D., Chairman and Chief Executive Officer of Novartis. So as a pilot, we have established multi-divisional management teams to run an integrated local business. Our customers in these countries are often structured the same way, and we believe we can hire better talent if we have a larger, more complex business to manage than separate local divisional units.

Several emerging geographies do not de facto distinguish between originator, generic and OTC drugs. With our broad Novartis product portfolio we are well-positioned to address the needs of patients for innovative medicines, prevention and affordable self- care options in the GEM countries says Andre Wyss, Head of Region Rest of World at the Pharmaceuticals Division but Head of GEM until December 1, 2008. Aligning promotional and commercial activities with synchronized initiatives for the total Novartis portfolio leads to increased presence and share-of-voice with key stakeholders, which ultimately improves awareness of our medicines.

This new model already has driven performance in various markets and allows for optimization of initial investments in countries where Novartis previously had a minimal presence. In 2008, aggregate year-on-year growth in GEM countries accelerated to 26%, compared to 11% the previous year.

In Malaysia, Novartis Pharmaceuticals was the strongest division, well supported by its line functions. But the creation of GEM opened an opportunity to use those resources to support and drive growth of other divisions and business units, for example, by drawing on relationships built through key account managers in the Pharmaceuticals Division. In other countries, GEM was able to benefit from the strong platform and contacts of Sandoz to expand the Oncology business faster and more efficiently than would have been possible from the outside.

We go out and can deliver a broad healthcare message, Mr. Wyss says. When the GEM country head meets the general manager of a hospital and explains that Novartis has innovative medicines, generics, vaccines and OTC self-medication products, we become a much more attractive partner.

In Jordan, the Pharmaceuticals Division and Sandoz were selling separately to the same key accounts. Today, GEM is approaching each institution with a single voice and positioning Novartis as a healthcare leader.

For example, oncology is the main focus at King Hussein Cancer Center in Amman, Jordan. But our needs extend far beyond oncology products to anti-infectives, painkillers and even simple OTC products, says Mahmoud Serhan, M.D., Chief Executive Officer of King Hussein Medical Center. In our decision-making process we prefer to deal with one face at a supplier. By combining the forces of all its divisions, Novartis has become an ideal partner, providing us with a wide range of healthcare solutions.

HEALTHY FAMILIES IN RURAL INDIA

Yet another cross-divisional experiment is under way in India, where a small Novartis team is attempting to build a self-sustaining business model catering to the health needs of low-income people living in rural villages. The initiative, called Arogya Parivar, or healthy family in Sanskrit, combines healthcare education with the sale of affordable Novartis products through local pharmacies.

An estimated 65% of the population of India has no access to medicine despite prices that are among the lowest in the world. Novartis has recognized the commercial potential of the fast-growing rural market that represents 70% of India s population and almost 60% of national disposable income.

Arogya Parivar set out to fill that vacuum. The mainstay of the initiative is a team of 200 health advisors who fan out to villages in four states. Each health advisor completes a training program for three to four diseases and we also train them in public speaking, says Olivier Jarry, Global Head Project Arogya from mid-2006 to mid-2008.

These health advisors are not Novartis employees. Some are experienced pharmaceutical sales representatives who moved from a city back to a village; some have backgrounds in fast-moving consumer goods; and some belong to local non-governmental organizations. The mix works very well, Mr. Jarry says.

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Training emphasizes ethical standards, particularly adherence to the Novartis Parma Promotional Practices Policy. We insist that our health advisors fulfill all Novartis standards and conduct themselves as if they were Novartis employees, Mr. Jarry says.

The initial focus of the initiative has been patient education: raising awareness about healthcare, hygiene and nutrition. The first step is having people become aware of diseases and how to treat or prevent them, Mr. Jarry says. That s what s most lacking in India: qualified doctors are rare and no one talks to people in the villages about diseases.

Arogya Parivar health advisors speak to villagers about diseases from tuberculosis and skin infections to asthma, allergies or diabetes. They help people in the village to recognize symptoms, Mr. Jarry says. Periodically we hold health camps and bring in doctors who do examinations on the spot and refer people diagnosed with a disease to a doctor for treatment. Attendance at one of our health camps can range from 200 to 2 000 people. If we skip the education part, we would miss 99% of potential patients.

The basic product portfolio promoted by Arogya Parivar health advisors includes prescription medicines and OTC self-medication products selected on the basis of both medical requirements of the rural poor and affordability. Weekly treatment costs are held below USD 1.25.

To enhance affordability, Novartis modified standard package sizes of products such as calcium tablets for pregnant women. We revived an old design of a tube holding 15 pills, half the number and half the price of our smallest standard pack. It s been a phenomenal success, Mr. Jarry says.

About 120 priority districts out of more than 600 districts across India have been selected for the initial phase of the Arogya Parivar program, based on criteria ranging from population and purchasing power to transportation infrastructure and density of private doctors. Operations currently span four Indian states, Mr. Jarry says. And by applying similar criteria, it would be possible to launch initiatives similar to Arogya Parivar in other countries, he adds.

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PHARMACEUTICALS OVERVIEW

KEY FIGURES **(In USD millions, unless indicated otherwise)**	**2008**	**2007**
Net sales	**26 331**	24 025
Operating income (1)	**7 579**	6 086
Return on net sales (%)	**28.8**	25.3
Research & Development	**5 716**	5 088
As % of net sales	**21.7**	21.2
Free cash flow	**7 679**	6 292
Net operating assets	**14 812**	13 984
Additions to property, plant & equipment (2)	**1 115**	1 436
Number of associates (FTE) (3) at year-end	**53 632**	54 613

(1) 2007 results include an exceptional USD 307 million restructuring charge for the Forward productivity initiative

(2) Excluding impact of business combinations

(3) Full-time equivalent positions at year-end

PORTFOLIO REJUVENATION

(% and total net sales in USD millions)

NEWS IN 2008

Accelerating momentum in Pharmaceuticals thanks to dynamic growth in Oncology, the portfolio of high blood pressure medicines and USD 2.9 billion of contributions from recently launched products.

Net sales rise 10% (+5% in local currencies) to USD 26.3 billion, led by solid performances in Europe, Latin America, Japan and priority emerging markets. In the United States, net sales fall 2%, but returns to solid growth in second half of 2008 while overcoming 2007 challenges from the start of generic competition for four medicines and *Zelnorm* suspension.

Operating income advances 25% on the business expansion and productivity gains as well as lower exceptional charges. Research and Development investments rise 12% to advance robust pipeline, while productivity gains support new product launches and expansion in emerging markets. Operating margin rises to 28.8% of net sales from 25.3% in 2007.

Oncology (USD 8.2 billion, +14% lc) provides four of the five top-selling medicines, led by *Gleevec/Glivec* at USD 3.7 billion. Cardiovascular strategic products (USD 6.7 billion, +10% lc) advance on gains from the new high blood pressure medicines *Exforge* and *Tekturna*, while *Diovan* reaches net sales of USD 5.7 billion.

Recently launched products provide increasing growth contributions in 2008, led by *Aclasta/Reclast*, *Tekturna/Rasilez*, *Exforge*, *Lucentis*, *Exelon* Patch, *Tasigna* and *Xolair* that together accounted for more than 10% of net sales in 2008.

Promising development pipeline with 152 projects: *Afinitor* (advanced kidney cancer), QAB149 (chronic obstructive pulmonary disease, or COPD) and ACZ885 (Muckle-Wells syndrome) submitted for regulatory approvals.

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Novartis is consistently rated as having one of the industry s most respected pipelines with 152 projects in clinical development. Several of these projects, which include potential uses of new molecular entities as well as additional indications or new formulations for marketed products, are for potentially best-in-class medicines that would advance treatment standards.

The following table provides an overview of selected projects.

GLOSSARY

Project/Compound Novartis brand name for marketed products *(in italics)* or project reference code (combination of three letters and three numbers) for compounds, which are individual molecular entities.

Generic name The official International Non-proprietary Name (INN) for an individual molecular entity as designated by the World Health Organization (WHO).

Indication A disease or condition for which a compound or marketed product is in development and studied as a potential therapy.

Mechanism of action Specific biochemical interaction through which a drug substance produces its pharmacological effect.

Formulation The way in which a medicine is administered, such as via a tablet, injection, skin patch, infusion or device.

Phase I First stage of testing in humans. At Novartis, proof-of-concept clinical trials are conducted in a homogeneous group of patients, defined either as a genetic disease or by biomarkers, to assess molecular understanding.

Phase II Following successful proof-of-concept results, confirmatory trials are performed in larger patient groups to further assess the efficacy and safety of how well a compound works, including at various doses and in various indications.

Phase III Final clinical trials before regulatory submissions to test a compound against a placebo or another medicine to determine definitive efficacy and safety in patients.

Submitted Comprehensive data provided to government regulators for marketing approval.

Therapeutic area	Project/compound	Generic name	Indication
Cardiovascular and Metabolism	*Tekturna* SPC (1)	aliskiren, valsartan most	Hypertension
	Galvus	vildagliptin	Type 2 diabetes
	Diovan/Starlix NAVIGATOR	valsartan, nateglinide	Prevention of new-onset type 2 diabetes, cardiovascular morbidity and mortality
	Tekturna SPC (1)	aliskiren, amlodipine, hydrochlorothiazide	Hypertension
	Tekturna ASPIRE HIGHER trials	aliskiren	Renal and cardiovascular events
	LCZ696		Heart failure
	LCI699		Heart failure
Oncology	*Afinitor* (RAD001)	everolimus	Renal cell cancer (lead indication), neuroendocrine tumors, solid tumors
	Tasigna	nilotinib	Gastrointestinal stromal tumor (lead indication), newly diagnosed chronic myeloid leukemia
	LBH589	panobinostat	Cutaneous T-cell lymphoma (lead indication), Hodgkin s lymphoma, hematologic tumors
	EPO906	patupilone	Ovarian cancer (lead indication) and other solid tumors
	SOM230	pasireotide	Cushing s disease (lead indication) acromegaly, neuroendocrine tumors
	Zometa	zoledronic acid	Adjuvant breast cancer
	PKC412	midostaurin	Aggressive systemic mastocytosis (lead indication), acute myeloid leukemia
	ASA404		Non-small cell lung cancer
Neuroscience and Ophthalmics	FTY720	fingolimod	Multiple sclerosis
	AGO178	agomelatine	Major depressive disorder
	Lucentis	ranibizumab	Diabetic macular edema
	AFQ056		L-dopa induced dyskinesia in Parkinson s disease
Respiratory	QAB149	indacaterol	Chronic obstructive pulmonary disease
	Xolair	omalizumab	Allergic asthma
	MFF258	formoterol, mometasone furoate	Asthma, chronic obstructive pulmonary disease
	NVA237	glycopyrronium bromide	Chronic obstructive pulmonary disease
	QVA149	indacaterol, glycopyrronium bromide	Chronic obstructive pulmonary disease
	Glivec	imatinib	Pulmonary arterial hypertension
	QMF149	indacaterol, mometasone furoate	Asthma, chronic obstructive pulmonary disease
	NIC002		Smoking cessation
Immunology and Infectious Diseases	ACZ885	canakinumab	Cryopirin-associated periodic syndrome (CAPS, lead indication), rheumatoid arthritis, systemic onset juvenile idiopathic arthritis
	Certican	everolimus	Prevention of organ rejection
	ABF656	albinterferon alpha 2-b	Chronic hepatitis C

SBR759		Hyperphosphatemia
SMC021	salmon calcitonin	Osteoarthritis (lead indication), osteoporosis
PTZ601		Hospital bacterial infections
Mycograb	efungumab	Invasive candida
AIN457		Psoriasis
AEB071	sotrastaurin	Prevention of organ rejection

(1) Single pill combination
(2) Breakpoint cluster region-Abelson fusion protein
(3) Important receptor tyrosine kinase protein
(4) Platelet-derived growth factor receptor protein

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Mechanism of action	Formulation	Planned submission dates	Phase I	Phase II	Phase III	Submitted
Direct renin inhibitor and angiotensin II receptor antagonist	Oral	Submitted US, 2009 EU	XXXXX	XXXXX	XXXXX	XXXXX
Dipeptidyl peptidase 4 inhibitor	Oral	Submitted US (approved EU)	XXXXX	XXXXX	XXXXX	XXXXX
Angiotensin II receptor antagonist and insulin secretagogue	Oral	2010	XXXXX	XXXXX	XXXXX	
Direct renin inhibitor, calcium channel blocker (CCB) and diuretic	Oral	2010	XXXXX	XXXXX	XXXXX	
Direct renin inhibitor	Oral	2010	XXXXX	XXXXX	XXXXX	
Dual angiotensin II receptor antagonist and neutral endopeptidase inhibitor	Oral	≥2012	XXXXX	XXXXX		
Aldosterone synthase inhibitor	Infusion	≥2012	XXXXX	XXXXX		
mTOR (5) inhibitor	Oral	Submitted US, EU	XXXXX	XXXXX	XXXXX	XXXXX
Bcr-Abl (2), c-Kit (3) and PDGFR (4) inhibitor	Oral	2009	XXXXX	XXXXX	XXXXX	
Deacetylase inhibitor	Oral	2009	XXXXX	XXXXX		
Microtubule depolymerization inhibitor	Infusion	2010	XXXXX	XXXXX	XXXXX	
Somatostatin analogue	Injection	2010	XXXXX	XXXXX	XXXXX	
Osteoclast inhibitor	Infusion	2010	XXXXX	XXXXX	XXXXX	
Signal transduction inhibitor	Oral	2011	XXXXX	XXXXX	XXXXX	
Tumor vascular disrupting agent	Infusion	2011	XXXXX	XXXXX	XXXXX	
Sphingosine-1-phosphate receptor modulator	Oral	2009	XXXXX	XXXXX	XXXXX	
MT1/MT2 (6) agonist and 5-HT2c (7) antagonist	Oral	2009	XXXXX	XXXXX	XXXXX	
Anti-VEGF (8) monoclonal antibody fragment	Intravitreal injection	2010	XXXXX	XXXXX	XXXXX	
Metabotropic glutamate receptor 5 antagonist	Oral	≥2012	XXXXX	XXXXX	XXXXX	XXXXX
Long-acting beta-2 agonist	Inhalation	Submitted US, EU	XXXXX	XXXXX	XXXXX	XXXXX
Anti-IgE monoclonal antibody	Liquid formulation for injection	Submitted EU, 2009 US	XXXXX	XXXXX		
Long-acting beta-2 agonist and corticosteroid	Inhalation	2009	XXXXX	XXXXX	XXXXX	
Long-acting muscarinic antagonist	Inhalation	2011	XXXXX	XXXXX		
Long-acting beta-2 agonist and long-acting muscarinic antagonist	Inhalation	2011	XXXXX	XXXXX		
Signal transduction inhibitor	Oral	2011	XXXXX	XXXXX		
Long-acting beta-2 agonist and corticosteroid	Inhalation	≥2012	XXXXX	XXXXX		
Nicotine Qbeta therapeutic vaccine	Injection	≥2012	XXXXX	XXXXX		
Anti-interleukin-1b monoclonal antibody	Injection	Submitted EU, US	XXXXX	XXXXX	XXXXX	XXXXX
Growth-factor-induced cell proliferation inhibitor	Oral	Submitted US, (approved EU, Japan)	XXXXX	XXXXX	XXXXX	XXXXX
Interferon alpha-type activity	Injection	2009	XXXXX	XXXXX	XXXXX	
Selective binding of phosphate (Fe(III) containing polymer)	Oral	2010	XXXXX	XXXXX		
Regulator of calcium homeostasis, inhibition of osteoclast activity	Oral	2011	XXXXX	XXXXX	XXXXX	
Carbapenem antibiotic	Infusion	2011	XXXXX	XXXXX		
Antibody fragment vs. fungal HSP90 (9)	Infusion	≥2012	XXXXX	XXXXX	XXXXX	

Anti-interleukin-17 monoclonal antibody	Lyophilisate in ampule	≥2012	XXXXX	XXXXX
Protein kinase C inhibitor	Oral	≥2012	XXXXX	XXXXX

(5) Mammalian target of rapamycin protein
(6) Melatonin receptor subtypes 1 and 2
(7) Serotonin receptor subtype 2c
(8) Vascular endothelial growth factor
(9) Heat shock protein 90

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MODELING THE FUTURE OF DRUG DEVELOPMENT

Novartis scientists are accelerating development of innovative medicines with cutting-edge tools and close cooperation among multi-disciplinary teams to translate fundamental science into treatments. Novartis leads the pharmaceutical industry in completing proof-of-concept studies to confirm a medicine s mechanism of action as well as exploring multiple disease indications before full development begins. A team of Modeling and Simulation specialists is adding competitive advantage by modeling the activity of medicines and vaccines to make better decisions and reduce the painfully high failure rate for new products in clinical trials.

The pipeline of new anticancer medicines at Novartis has expanded rapidly in recent years and during 2008 six innovative drugs reached the pivotal phase of clinical testing a period of intense productivity virtually unprecedented in the field of oncology.

A key milestone came in September when the US Food and Drug Administration (FDA) granted a priority review to *Afinitor* for treatment of patients with advanced kidney cancer who have failed standard treatment. Priority reviews are expedited timelines for FDA evaluation, reserved for therapies with potential to fill significant unmet medical need.

After *Afinitor* was accepted for priority review, the FDA requested clarification of certain data as well as additional data from an ongoing trial in pancreatic neuroendocrine tumors. As a result, *Afinitor* is expected to receive a regulatory decision from the FDA within the first quarter of 2009 for patients with advanced kidney cancer.

Following a separate priority review, the FDA approved *Gleevec/Glivec* as the first therapy to reduce recurrence of gastrointestinal stromal tumors (GIST) after surgery. *Gleevec/Glivec*, a pioneering targeted anticancer medicine from Novartis, already is approved to treat chronic myeloid leukemia, primary GIST and other types of rare tumors.

Regulatory applications for *Afinitor* and *Gleevec/Glivec* also have been filed in the European Union, Switzerland and other countries, and currently are under review.

In addition to late-stage projects, we have a number of exciting early compounds in the oncology pipeline, says David Epstein, Head of the Oncology Business Unit and the new Molecular Diagnostics business at the Novartis Pharmaceuticals Division. Some of those new compounds such as our PI3 kinase inhibitors are first-in-class and have a chance to redefine cancer care across multiple tumor types.

Research and Development teams at Novartis cooperate closely to translate fundamental science into new medicines. The Translational Science group serves as the vital bridge for this teamwork, leading multidisciplinary teams in initial proof-of-concept studies of new medicines in patients. These proof-of-concept studies are designed to confirm the medicine s mechanism of action and explore multiple disease indications before full development begins.

Novartis scientists are accelerating the development of innovative new medicines with cutting-edge tools. Novartis Oncology has built a powerful team to identify and develop biomarkers substances or functions in the body that can be measured to demonstrate safety and efficacy of a medicine, or to identify patients most likely to respond positively to treatment. Biomarkers are a cornerstone of efforts by Novartis to deliver superior treatment. We believe that this is the future of Oncology, and Novartis is addressing that future today, Mr. Epstein says.

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Translational Science also underpins drug development outside the Oncology business, in therapeutic areas known collectively as General Medicines. Trevor Mundel, M.D., Global Head of Development at the Novartis Pharmaceuticals Division, has realigned management, streamlined decision-making and introduced new technologies since taking the helm in early 2008.

Benchmarking studies show that Novartis is the fastest company in the industry by a substantial margin in reaching proof-of-concept, Dr. Mundel says. Yet even if Translational Science has brought us a long way beyond where we were previously, the full impact cannot be realized without addressing the other pieces of the puzzle.

Lean and nimble biotech-style teams that drive early development at Novartis are remarkably effective in confirming whether a new drug works in somebody, somewhere, he adds. But you can t have a highly flexible entity like that tagged onto an entirely rigid, massively bureaucratic end pipe. We have to become leaner and more flexible in our approaches to late stages of development.

Dr. Mundel has delegated a pivotal role to the Modeling and Simulation team at Novartis, one of the largest of its kind in the pharmaceutical industry. The concept is simple: If Boeing and Ferrari can test their engineering feats on the computer before actually building planes and cars, Novartis can model diseases and the activity of medicines and vaccines to make better decisions and lower the painfully high failure rate for new medicines in clinical trials.

The Modeling and Simulation team already is contributing to high-priority development programs in the General Medicines pipeline such as ACZ885, a monoclonal antibody being developed as a treatment for multiple inflammatory disorders. Modeling and Simulation has become the key link between what we do in early exploratory development and the later stages of confirmatory testing, Dr. Mundel says.

For many diseases you can come up with quite nice models of what typically might happen. And because you can do that across some of the most interesting diseases we work in, sparse data that come out of Translational Science can be integrated into the model, he adds. It can give much better utility than the traditional, empirical trial-and-error approach.

AFINITOR: IN THE *GLEEVEC/GLIVEC* MOLD

Afinitor, under investigation for several cancer indications including advanced kidney cancer, epitomizes the new generation of targeted anticancer agents from Novartis modeled on the success of *Gleevec/Glivec*. *Afinitor* works by blocking the function of a protein called mTOR, a master switch in cells that serves as a hub for multiple signaling and metabolic pathways.

The mTOR pathway is mission control for proliferation in virtually every cell in the body, says Jeff Porter, Ph.D., Head of the Development and Molecular Pathways Platform at the Novartis Institutes for BioMedical Research (NIBR). Normally, mTOR is kept under tight control in the cell. But mutations in genes or other biological defects can jam the pathway in the on position, triggering the uncontrolled cell growth and proliferation characteristic of cancer.

It has taken decades to unravel the complex connections between mTOR and cancer-related pathways. *Afinitor* was developed initially as an immunosuppressant to prevent rejection of organ transplants and has been approved for that indication under the brand name *Certican* in more than 40 countries. Novartis began parallel development of *Afinitor* in cancer in 2002. The clinical program focused on patients with advanced kidney cancer who had failed standard

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therapy with treatments targeting the vascular endothelial growth factor (VEGF) pathway.

VEGF pathway inhibitors suppress angiogenesis growth of new blood vessels that tumors need to grow. *Afinitor* hits the VEGF pathway as well, but in a different way and further upstream in the tumor cell, says David Lebwohl, M.D., Head of the *Afinitor* clinical program at Novartis Oncology.

The growing numbers of patients who have failed standard therapy for advanced kidney cancer represent a pressing, unmet medical need. These are patients who have no treatment option, says Alessandro Riva, M.D., Head of Oncology Global Development.

In a study called RECORD-1, the pivotal Phase III trial on which regulatory submissions for *Afinitor* are based, patients whose cancer had worsened despite prior treatment were randomized to receive either *Afinitor* or placebo, an inactive substance made to appear like a medicine. Treatment in both groups continued until cancer once again began to progress. Initial results of RECORD-1 showed treatment with *Afinitor* more than doubled time without tumor growth and reduced the risk of disease progression by 70%. Due to the strength of these initial results, patients in the placebo group were allowed to cross over and begin treatment with *Afinitor*.

Updated results from RECORD-1 presented at the European Society for Medical Oncology Congress in September showed patients receiving *Afinitor* had no tumor growth for nearly five months versus 1.9 months for patients in the placebo group. Importantly, 25% of patients who received *Afinitor* still had no tumor growth after 10 months of treatment.

In a commentary accompanying publication of RECORD-1 results in the UK medical journal Lancet, Jennifer Knox, M.D., assistant professor of medicine at the University of Toronto, observed: A 70% reduction in the risk of disease progression or death is impressive among studies for any advanced cancer and was better than expected [for RECORD-1]. Although some questions remain unanswered, Dr. Knox added: This is strong evidence to support the anti-tumor activity of [*Afinitor*] in this population.

FROM SEQUENTIAL TO PARALLEL

The studies in renal cancer are just the beginning. The program is spearheading an initiative by Novartis Oncology for *Afinitor* to accelerate development of promising new medicines. We re taking a program that used to be fairly sequential and moving up studies in parallel to maximize the opportunity for patients, Mr. Epstein says.

During the past 18 months, Dr. Riva and Novartis medical directors around the world have coordinated studies of *Afinitor* in multiple additional indications. We now have positive results in about a half-dozen indications and we are initiating clinical trials across almost all of them, Mr. Epstein says. It s an example of the urgency we want to instill in our global Development organization. Those new indications range from breast cancer and pancreatic neuroendocrine tumors to gastric cancer and tuberous sclerosis complex, a rare genetic disorder that causes tumors to form in the brain and kidneys, and in severe cases can lead to mental retardation.

At the same time, the success of *Afinitor* in renal cancer offers a key proof-of-concept for another major development program at Novartis targeting PI3 kinase, a large family of enzymes that are important regulators of growth, proliferation and survival in virtually all cells. The PI3 kinase program at Novartis began in the late 1990s and initially focused on respiratory and autoimmune diseases. Those early programs were soon overshadowed by mounting evidence of a link between the PI3 kinase pathway and cancer. The pathway is activated when growth factors bind to receptors on the cell surface. A biological chain reaction carries the signal to the nucleus of the cell, where it stimulates synthesis of proteins needed for growth or nudges the cell-cycle machinery to initiate cell division.

Importantly, mTOR appears to be a node in the downstream branch of the PI3 kinase pathway. Novartis is the only major pharmaceutical company developing medicines targeting both the upstream (PI3 kinase) and downstream (mTOR) branches of the pathway.

The programs reflect a central tenet of NIBR research strategy: attacking multiple targets within a pathway believed to play a major role in a disease like cancer. Two PI3 kinase inhibitors discovered by Novartis have entered early development. Both target PI3 kinase as well as mTOR, while a later generation of more selective PI3 kinase inhibitors is still in preclinical development. There have been lots of debates about whether you want specificity or a dual PI3 kinase/mTOR inhibitor, says William Sellers, M.D., Head of Oncology Research at NIBR. Suffice to say that there are good reasons to have both.

COMBINATIONS AND BIOMARKERS

Combinations incorporating multiple anticancer agents have been the mainstay of oncology for decades, and combinations play a significant role in development programs at Novartis Oncology. Patients need combinations because there are multiple pathways helping their cancers grow, Mr. Epstein says. If you can knock out multiple pathways, there is more chance patients will respond better and live longer.

The broad mechanism of action for *Afinitor* makes it a potential component in many combinations. We are testing multiple opportunities in combination with current standards of care across different tumor types and different phases of the disease, Dr. Riva says. Our priority is to

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make every effort to improve the treatment of patients, and if we can achieve this through a combination of a Novartis drug with one from another company, we are happy to do that.

Novartis and Swiss rival Roche Holding AG have exchanged supplies of medicines for testing as possible combinations, including *Afinitor* with Avastin®, a blockbuster VEGF inhibitor jointly developed by Roche and Genentech Inc. I think we ll see more of this, Mr. Epstein says. As combinations become increasingly important in the treatment of cancer, companies somehow need to work together so that clinical trials of combinations can start as early as possible.

The aggressive biomarker development program at Novartis also is expected to help make new medicines available to patients faster. In late 2008, Mr. Epstein was tapped to lead a new unit focusing on development of innovative molecular diagnostics based on biomarkers.

Changes in biomarkers can be detected earlier or more readily than traditional clinical endpoints, though results based on surrogate markers normally need to be confirmed by long-term outcomes studies.

Another potential application is predicting patient response to drug treatment. Among patients sharing a common diagnosis, some may respond to a medicine while others fail to respond and a third group develops side effects. Unraveling the reason for differences in individual response would enable companies to develop diagnostic tests to help identify those patients more likely to respond to treatment, as well as those more likely to develop side effects.

The need to find surrogate endpoints and biomarkers has been clear in oncology for a long time, Mr. Epstein says. We ve been able to take a big step forward and we have biomarker programs in place for almost every drug that we have in the clinic.

GLEEVEC/GLIVEC AND *TASIGNA*: AN ALLIANCE WITH PATIENTS

The potential new indications for *Gleevec/Glivec*, including adjuvant treatment of GIST, underscore a continued commitment by Novartis to cancer patients with limited treatment options. Another example of that commitment is the development of *Tasigna*, a treatment for patients with chronic myeloid leukemia (CML) who are resistant or intolerant to existing therapies, including *Gleevec/Glivec*.

Tasigna was approved by the United States, the European Union and other countries in 2007. Approval of *Tasigna* provides more comprehensive treatment options for physicians and patients, Mr. Epstein says.

Development was exceptionally rapid: *Tasigna* went from first human trials to regulatory submissions in slightly more than two years. We were able to build on our *Gleevec/Glivec* experience, Dr. Riva says. And just as *Gleevec/Glivec* expanded from initial approval in CML to an

unprecedented number of additional indications, clinical trials have been launched to compare *Tasigna* with *Gleevec/Glivec* in patients with various forms of CML, as well as GIST.

Meanwhile, Novartis Oncology has introduced the CML Alliance, a package of diagnostic tests, programs and materials to enhance patient adherence, help improve outcomes and potentially extend the lives of leukemia patients. These tests, in turn, help physicians reach better outcomes for patients, Mr. Epstein says. Physicians would not normally have access to these tools. By putting them into the hands of doctors who actually use them, we make a real difference and distinguish Novartis from other companies.

The CML Alliance package includes tests for blood-level monitoring of patients treated with *Gleevec/Glivec*, enabling physicians to individualize dosage. Metabolism varies among individuals, and we realized that patients receiving identical doses of *Gleevec/Glivec* had different levels of the drug in their blood, Mr. Epstein adds. That s important because blood levels correlate with outcomes: Most patients with high drug levels do much better than patients with low levels.

In addition, Novartis has worked with the European Leukemia Net, a network of academic institutions and researchers, to develop standard guidelines for treatment of CML patients through the entire cycle of the disease. The guidelines have been widely adopted around the world. In 2009, Novartis plans to launch similar packages for GIST and neuroendocrine tumors, based on the initial CML Alliance model.

GENERAL MEDICINES: A NIMBLE ALTERNATIVE

In both Oncology and General Medicines, Novartis has eluded the declining productivity that has afflicted many rivals in recent years. Between 2000 and 2008, Novartis received the most FDA approvals for new molecular entities of any major pharmaceutical company.

The contribution of Translational Science has enabled Novartis to halve the average time required to reach proof-of-concept in clinical programs. Dr. Mundel is convinced that further improvement can be achieved during Phase II studies in which companies traditionally test a range of doses of a new medicine in search of initial indications of efficacy that can be confirmed in the pivotal Phase III trials.

Phase II is choking the industry, Dr. Mundel says. Often Phase II trials are actually bigger and take longer than Phase III studies, he says. And the failure rate for Phase II across the industry is extraordinarily high

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approaching 80%, according to the latest benchmarking numbers.

Novartis fares better than the industry average because drugs that do not work are filtered out earlier. But the early proof-of-concept strategy also poses challenges. Typically, our early proof-of-concept studies are done in relatively small groups of patients, so the data are sparse. How do we project that into big programs? Dr. Mundel adds.

The traditional answer for pharmaceutical companies would be a huge Phase IIB study. At Novartis, however, Modeling and Simulation provides a more nimble alternative.

Modeling and simulation begins with the creation of a mathematical and statistical model of a medicine acting in parts of the body where the disease occurs. Modelers use data from actual patients, literature data and preclinical animal data to build models, then statistically predict responses to the medicine over time.

In some programs, modeling and simulation can be a springboard directly from the proof-of-concept to Phase III. Our goal is to omit Phase IIB in up to 50% of our programs. In the remaining programs, modeling and simulation will help usto reduce the size, duration and cost, Dr. Mundel says. This is the extension of what people have always hoped to do: rational drug development, or Model-Based Drug Development, to use a term coined by the FDA.

As a Rhodes Scholar, Dr. Mundel studied mathematics at the University of Oxford and later completed graduate studies in mathematics at the University of Chicago. He is rigorous about distinguishing useful applications of modeling and simulation from exaggerated claims made by some proponents.

Models have to be infused with data and a lot of common sense and judgment. They really are dependent on how much you know about the disease and about the precedent for the drug and its mechanism of action, he cautions.

There also are elements of modeling and simulation that approximate guesswork. In particular, modeling and simulation has gotten wrapped up with the hype around systems biology. We aren t trying to model the complete, complex pathway dynamics of systems, which remain highly speculative. We re talking about modeling select components of drug pathways and the more familiar models of pharmacokinetics and pharmacodynamics.

FROM HIGH SCIENCE TO MARKET RESEARCH

The Modeling and Simulation organization at Novartis is headed by Donald R. Stanski, M.D., who, following an academic career in anesthesiology/clinical pharmacology at Stanford University, served as a scientific advisor to the director of the FDA s Center for Drug

Evaluation and Research before joining Novartis in 2005.

Basically we integrate pieces of information in a way that uses mathematics and statistics as a thread to bind, Dr. Stanski says. We want to integrate every piece of knowledge and data to make smarter decisions about whether a molecule is worth developing, and decrease the clinical-trial failure rate in Phase III.

Applications of modeling and simulation at Novartis range from esoteric high science to market research and health economics. To support development of a novel medicine for spinal cord injury, Dr. Stanski s team simulated circulation of spinal fluid, incorporating pulsations generated by heartbeat and respiration, and adjusting the model for the effect of spinal nerve roots on the flow path. The model resolved key questions about administration of the treatment into the spinal space.

Modeling and Simulation also is beginning to work closely with Strategic Marketing on development compounds, assisting in

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preparation of outcomes and health economic analysis, and integrating with portfolio analysis. Still, some of the clearest examples yet of the potential impact of modeling and simulation have come in priority development programs, including the promising monoclonal antibody ACZ885.

ROAD TO REMISSION

ACZ885 targets IL-1 beta, a key weapon in the body s immune system defenses. Excessive production of IL-1 beta is believed to play a role in diseases ranging from rheumatoid arthritis and chronic obstructive pulmonary disease to asthma and certain rare genetic diseases.

Novartis scientists chose to conduct the initial proof-of-concept study in patients with Muckle-Wells syndrome, a rare inherited disease in which a genetic mutation stimulates excess production of IL-1 beta and causes itching skin rashes, daily fever and swollen joints. (Muckle-Wells syndrome and two related disorders are known collectively today as cryopyrin-associated periodic syndromes, or CAPS.)

Muckle-Wells syndrome seemed an ideal candidate for the proof-of-concept because its pathology was uncomplicated, driven by a single, well-defined molecular defect. According to the scientific hypothesis, ACZ885 should bind exclusively with IL-1 beta circulating in the blood, halting excessive production and alleviating symptoms.

In late 2004, Timothy Wright, M.D., and Thomas Jung, M.D., from the Novartis Translational Science Group contacted Professor Philip Hawkins at London s Royal Free and University College Medical School, a world authority on rare diseases such as MuckleWells syndrome. A proof-of-concept study was jointly designed and the first patient received ACZ885 in early 2005. Three more patients were given injections of ACZ885, and all had immediate positive responses lasting, on average, about six months.

Subsequent trials have provided even more evidence of the safety and efficacy of ACZ885 in this rare disease. To date, 69 patients have received the drug, and treatment of the very first patient has continued for more than 3.5 years.

Behind the scenes, the Novartis Modeling and Simulation team, led by Philip Lowe, Ph.D., has played a crucial role in the ACZ885 program. It is the clearest example yet of how modelers can extrapolate sparse data from initial proof-of-concept studies to predictions about larger patient populations or different diseases.

Following the initial study in Muckle Wells syndrome in 2005, the Modeling and Simulation group analyzed data about the action and effects of the treatment in the body; how it is absorbed, metabolized and eliminated; and other measures of patient response.

One key question was whether ACZ885 would merely neutralize IL-1 beta or actually achieve a disease-modifying effect on patients with Muckle-Wells syndrome. Surprisingly, the resulting model indicated ACZ885 was able to decrease the IL-1 beta pathway to near normal for

about six weeks after a single treatment. Modelers then calculated that a single injection every eight weeks would hold the IL-1 beta pathway in check and keep patients with Muckle-Wells syndrome in full remission.

Applying these predictions based on data from only four patients ACZ885 advanced to a confirmatory trial. After achieving clinical remission following a single dose of ACZ885, a total of 31 patients were randomized to receive either three additional injections of ACZ885, eight weeks apart, over the following six months or the identical schedule of placebo injections.

The Modeling and Simulation group predicted none of the patients receiving ACZ885 would suffer flares, or recurrence of active disease, while more than 90% of the control group would have flares. In fact, all patients treated with ACZ885 did remain flare-free during the trial; 81% of the control group suffered recurrences.

This is our Phase III study and the outcome is an example of how powerful modeling and simulation can be for the design of clinical trials, Dr. Jung says. The data provided the foundation of regulatory applications for ACZ885 submitted to authorities in Europe and the US in 2008.

Meanwhile, in line with research strategy at Novartis, the ACZ885 program has expanded to parallel disease indications following the initial successful proof-ofconcept trial. Currently, ACZ885 is being tested or explored as a potential treatment for rheumatoid arthritis, systemic onset juvenile idiopathic arthritis and several other indications.

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AFQ056: PROBING FUNDAMENTAL MECHANISMS IN THE BRAIN

Diseases affecting the brain or central nervous system pose formidable hurdles in drug discovery. In the 1990s Novartis was one of the first major pharmaceutical companies to show an interest in a new family of brain receptors, known as mGluRs. AFQ056, a compound generated by Novartis chemists directed at the receptor target mGluR5, is in clinical trials for treatment of a complication related to therapy for Parkinson s disease. The AFQ056 program is an example of how use of drug candidates can be rapidly re-directed as more is learned about the mechanisms of disease.

Drug discovery rarely is an overnight success.

In 1990, a team of Japanese researchers identified a new class of receptors in the human brain, setting off a scientific race to translate the discovery into new medicines for disorders ranging from drug addiction and anxietyto schizophrenia and Parkinson s disease.

Novartis was one of the first major pharmaceutical companies to show an interest in the new family of metabotropic glutamate receptors, known by the acronym mGluRs. Novartis scientists generated a series of compounds directed at this target. One of these compounds, AFQ056, is directed to a specific subset of the mGluR family, termed mGluR5. An inhibitor of mGluR5, AFQ056 currently is in clinical trials for a complication of therapy for Parkinson s disease.

The story of AFQ056 reflects the innovative research strategy at Novartis. Scientists at the Novartis Institutes for BioMedical Research (NIBR) focus on both where the scientific knowledge leads, and where there is an unmet patient need. As science evolves and more is learned about the mechanisms of disease, the use of drug candidates may be rapidly redirected. The original hope for mGluR5 inhibitors was to treat anxiety. Because anxiety is a very heterogeneous disease in terms of mechanism, however, diseases with a more specific linkage to mGluR5 were sought.

Our approach is to go after diseases where there is unmet need, and we believe we understand enough about the fundamental mechanism to make an impact, says Mark Fishman, M.D., President of NIBR and member of the Executive Committee of Novartis. Once we show a medicine is safe and effective in a homogeneous population, we extrapolate that to subsets of more common diseases.

AFQ056 exemplifies that approach. Scientists from NIBR and the Translational Medicine team that directs early development tested AFQ056 in a series of proof-of-concept studies in humans and steadily narrowed the focus of the program. Based on rodent models and human post-mortem data, the team focused on Parkinson s disease levodopa-induced dyskinesia (PD-LID) as a target indication.

DISORDER OF MOVEMENT

Parkinson s disease is a disorder that usually strikes between the ages of 50 and 60. The hallmarks of Parkinson s disease are disorders of movement. Patients have a hard time initiating movement, steps become short and shuffling, and balance is impaired. Muscle stiffness limits movements and problems with speech are common. Tremor is also common, especially of the hand.

Symptoms of Parkinson s disease appear when brain cells that produce the neurotransmitter dopamine die or become impaired. Standard treatment today is dopamine-replacement therapy with levodopa,

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a natural substance that is converted to dopamine once inside the body. The introduction of levodopa in the 1960s was a revolutionary step in overcoming the symptoms of Parkinson s disease. Novartis has established expertise in the field of Parkinson s disease and markets *Stalevo*, an innovative treatment that combines levodopa with inhibitors of critical metabolizing enzymes.

Unfortunately, the majority of patients treated chronically with levodopa develop dyskinesias, rapid, irregular involuntary movements such as flinging and flailing arms which can be as crippling as the underlying disease. According to the Michael J. Fox Foundation, founded by the Canadian actor who has emerged as a leading spokesman for Parkinson s disease, approximately 80% of patients develop dyskinesias after five to 10 years of treatment with levodopa.

These dyskinesias are particularly prominent among younger Parkinson s disease patients. No effective treatment for levodopa-induced dyskinesias is yet available, and severe cases are treated with surgical methods such as deep brain stimulation. Gaining insight into ways to control or prevent dyskinesia would make a dramatic impact on the daily lives of Parkinson s patients, according to Deborah W. Brooks, a co-founder of the foundation.

PD-LID illustrates the triad of qualities we look for in a proof-of-concept study: a high unmet medical need, compelling scientific rationale and a sound medical hypothesis that can be rigorously tested in patients, says neurologist Donald R. Johns, M.D., Head of Neuroscience Translational Medicine at NIBR.

The AFQ056 project really took off after colleagues from Translational Medicine identified PD-LID as a potential indication, adds Fabrizio Gasparini, Ph.D., the chemist who led the team that discovered AFQ056 and recipient of a 2006 Novartis leading scientist award for his contributions to the program.

Diseases affecting the brain or central nervous system pose exceptional hurdles in drug discovery. We don t understand the physiology of the brain as well as we do other organs. And most major neurological diseases are chronic, debilitating disorders that progress slowly over decades. The triggers are still unknown and we lack effective diagnostic tools, Dr. Gasparini says.

It s also a challenge to deliver medicines into the brain. A barricade of densely packed cells known as the blood-brain barrier protects the brain from common bacterial infections, but it also prevents passage of potentially beneficial treatments. Even when a medicine is able to penetrate the blood-brain barrier, it is difficult to monitor the effects in the brain following treatment, Dr. Gasparini adds. An imaging technique developed by NIBR colleagues showed that AFQ056 penetrates into the brain and binds with mGluR5, and permitted better dosing decisions. That tool has been crucial to the success of the program so far. Still, formidable hurdles remain.

FINE-TUNING GLUTAMATE SIGNALS

Every idea, memory and emotion produced by the human brain is created as a series of electrical and chemical signals transmitted through connected networks of neurons. Neurons transmit these signals to one another at specialized sites of contact called synapses, junctions between two nerve cells. A synapse relays information by releasing chemical messengers, called neurotransmitters, from the sending neuron to the

receiving one where the neurotransmitter binds to related receptors, fitting snugly like a key in a lock. One of the most important neurotransmitters is glutamate, which acts by binding to the glutamate receptors, including the mGluR family.

Proper function of the brain depends on a delicate balance of signaling between excitatory and inhibitory neurotransmitters. Glutamate is one of the principal excitatory neurotransmitters. Too much glutamate signaling leads to imbalances believed to play a role in diverse brain disorders.

mGluR5 is present at key nodes in brain circuitry and under normal conditions and circumstances, mGluR5 functions to fine- tune glutamate transmission, says Graeme Bilbe, Ph.D., Global Head for the Neuroscience Disease Area at NIBR. Inhibition by AFQ056 offers an effective way to modulate the excessive glutamate transmission occurring in the brain regions involved in Parkinson s disease.

As development of AFQ056 progressed, discoveries in fundamental science added support to the hypothesis that levodopainduced dyskinesias were due to excessive mGluR5 signaling. Preparations for the proof-of-concept study of AFQ056 in the treatment of PD-LID were reinforced by the arrival of Baltazar Gomez-Mancilla, M.D., as the Translational Medicine representative on the AFQ056 team. Dr. Gomez-Mancilla brought a unique set of skills in the basic science, clinical expertise and drug development of Parkinson s disease to our interdisciplinary scientific and clinical team, Dr. Johns says.

The successful proof-of-concept study of AFQ056 was completed in May 2008. The dyskinesias were diminished in most patients. While early observations are quite encouraging, this short-term study needs verification in full development. In addition, the proof-of-concept in dyskinesias suggests potential benefit of AFQ056 in treatment of a broader spectrum of disorders linked anatomically with the basal ganglia, the region of the brain that controls movement.

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VACCINES AND DIAGNOSTICS OVERVIEW

KEY FIGURES **(In USD millions, unless indicated otherwise)**	**2008**	**2007**
Net sales	**1 759**	1 452
Operating income	**78**	72
Return on net sales (%)	**4.4**	5.0
Research & Development	**360**	295
As a % of net sales	**20.5**	20.3
Free cash flow	**-226**	-91
Net operating assets	**4 984**	4 801
Additions to property, plant & equipment(1)	**435**	287
Number of associates (FTE)(2) at year-end	**4 774**	4 810

(1) Excluding impact of business combinations

(2) Full-time equivalent positions at year-end

VACCINES DEVELOPMENT PIPELINE

(1) Japanese encephalitis vaccine

(2) H5N1 vaccine intended for use before a pandemic outbreak

(3) Neisseria meningitidis bacteria serogroups A, C, W-135 andY

(4) Flu cell-culture vaccine

(5) Neisseria meningitidis bacteria serogroup B

(6) Collaboration with Intercell (7)Group B Streptococcus

(8) Cytome galovirus, collaboration with AlphaVax

(9) Hepatitis C virus; therapeutic and prophylactic vaccine

(10) Human immunodeficiency virus

NEWS IN 2008

Solid expansion in 2008 supports major investments to advance novel meningitis vaccines as well as to improve manufacturing quality and capacity following 2006 acquisition of Chiron.

Net sales advance 21% (+20% in local currencies) to USD 1.8 billion. Key growth drivers are H5N1 pandemic influenza vaccine deliveries to the US government, pediatric vaccines and steady growth in the diagnostics business.

Operating income advance on higher vaccines volumes and a better product mix that support major Research and Development investments and manufacturing improvement initiatives.

US and EU submissions completed in 2008 for *Menveo* vaccine targeting deadly meningococcal meningitis serogroups A, C, W-135 and Y in patients from age 11 to 55. Trials are underway in children from age two months to ten years. New data in 2008 suggest MenB vaccine, now in Phase III trials, has potential to be first to protect infants as young as six months from B serogroup.

Diagnostics refocuses in 2008 on success in preventing spread of infectious diseases through blood-testing tools. Novartis Molecular Diagnostics, a new business created in 2008 in the Pharmaceuticals Division, to lead Group initiatives in medicine- related diagnostics.

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VACCINES AND DIAGNOSTICS

During 2008, regulatory applications were submitted in Europe, the United States and other countries for *Menveo*, the first of two meningococcal disease vaccines from Novartis in advanced stages of clinical testing. With the broadest portfolio of meningococcal vaccines, Novartis is dedicated to preventing infection from this deadly disease in infants, children and adults worldwide.

The transformation of the Novartis Vaccines and Diagnostics Division advanced in strategic areas during 2008, from regulatory applications for *Menveo*, a promising investigational vaccine against meningococcal disease, to the expansion of production capacity for existing vaccines and in preparation for new launches.

We are building a world-class platform for further growth, says Joerg Reinhardt, Ph.D., Chief Operating Officer of Novartis and member of the Executive Committee of Novartis, who headed the Vaccines and Diagnostics Division until December 1,2008. The vaccine market is set to expand for many reasons: new disease targets, new scientific tools to develop vaccines against those targets, and vaccination of broader age groups adolescents, adults and the elderly.

With its focus on prevention, Vaccines and Diagnostics fits neatly within the diversified healthcare portfolio of Novartis. Along with fields of scientific research that overlap with the Pharmaceuticals Division, Vaccines and Diagnostics benefits from the long experience in biotechnology production at Sandoz, our generic pharmaceuticals Division.

Healthcare is shifting to prevention, and vaccines are an excellent complement to therapeutic medicines, Dr. Reinhardt says. In addition, vaccines have strong support from payors because prevention of disease is almost always more cost-effective than treatment.

MEN VEO: FILLING UNMET NEED

Key milestones in 2008 included the submission of regulatory applications in Europe, the United States and other countries for the investigational vaccine *Menveo*, for vaccination of people from 11 to 55 years of age. *Menveo* is the first of two meningococcal disease vaccines from Novartis at advanced stages of development. The successful launch of *Menveo* and our pioneering meningococcal type B vaccine could potentially save thousands of lives and may provide a steady source of revenue, allowing us to continue investing in our pipeline to discover and develop even more life-saving vaccines in the years to come, Dr. Reinhardt says.

In clinical trials, the *Menveo* investigational vaccine has been shown to elicit a protective immune response against four of the most common serogroups A, C, W-135 and Y of Neisseria meningitidis, also known as meningococcus. These serogroups can cause potentially deadly bacterial infections and account for most cases of meningococcal disease worldwide. Most of the remaining cases are caused by an elusive B serogroup (MenB) of N. meningitidis. The prevalence of N. meningitidis serogroups varies from country to country. In North America, there is a mix of B, C and Y strains, while in the so-called Meningitis Belt across central Africa, 80% of cases are caused by serogroup A. In Argentina,

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serogroup B accounts for 65% of infections; in Brazil, 70% of cases are caused by serogroup C; and recently in Saudi Arabia, serogroup W-135 has accounted for up to 80% of cases.

More than 14 000 people have been vaccinated with *Menveo* during the clinical development program to date. The vaccine also has been shown to elicit a protective immune response in infants, the group most susceptible to meningococcal infections. No currently available quadrivalent vaccine containing four components that stimulate immune responses against different serogroups has demonstrated a strong and lasting immune response for this age group.

Data published in 2008 in the Journal of the American Medical Association (JAMA) showed that *Menveo* generated protection against the four serogroups of N. meningitidis using a vaccination schedule beginning at two months of age. As the first meningococcal vaccine to elicit a strong immune response in infants, *Menveo* could potentially fill a large unmet medical need. Regulatory applications for vaccination of infants with *Menveo* are expected to be submitted to authorities in the European Union in 2009 and in the United States in 2010.

In an editorial accompanying the JAMA publication, Lee Harrison, M.D., Professor of Medicine at the University of Pittsburgh, said the *Menveo* study represents a substantial advance in the vaccine prevention of meningococcal disease because it provides evidence for a well-tolerated and immunogenic conjugate vaccine for infants.

Separately, Novartis presented results of a head-to-head trial of *Menveo* and Menactra®, a quadrivalent vaccine available only in the United States. Menactra® was developed by the Sanofi Pasteur unit of French pharmaceutical group Sanofi-aventis SA.

In the study, adolescents immunized with *Menveo* generated higher levels of antibodies than Menactra® against the A, C, W-135 and Y serogroups; however these higher levels do not necessarily imply that *Menveo* is more protective than Menactra®. In a notable result for serogroup Y among adolescents with low levels of immunity at the time of vaccination, 81% of subjects receiving *Menveo* generated a protective immune response versus 54% of subjects receiving Menactra®.

The US Centers for Disease Control and Prevention recommend routine immunization with a quadrivalent meningococcal vaccine for all adolescents between the ages of 11 and 18 as well as college students living in dormitories and people in other high-risk groups.

PIONEERING SCIENCE

In his JAMA editorial, Dr. Harrison cautioned that despite progress toward comprehensive worldwide prevention of meningococcal disease, much work remains to be done because there still is no broadly protective vaccine against Men B. Novartis is racing to fill that gap with a pioneering MenB vaccine that is a prototype for the use of genomics in vaccine discovery.

Starting with the genome sequence of N. meningitidis, Novartis researchers used computers to search for similarities to known genes and uncovered dozens of potential targets either secreted by the pathogen or located on the bacterial cell surface where they can stimulate an immune response. The list of candidate antigens, or proteins that stimulate immune reactions, was narrowed to three major antigens. These were combined into the multi-component MenB vaccine that has now reached Phase III clinical trials in the European Union, the pivotal round of clinical testing required for regulatory licensure.

More than 20 000 infants will receive the MenB vaccine during the clinical development program. In 2008, Novartis presented results from two studies that supported the vaccine s potential to provide broad coverage to both younger and older infants. MenB causes about 70% of meningococcal disease in Europe and about a third of cases in the United States; infants and toddlers comprise the age group most at risk.

With the broadest development portfolio of meningococcal vaccines in the industry, Novartis is dedicated to preventing infection from the five major causes of this deadly disease in infants, children and adults around the world, Dr. Reinhardt says.

PRODUCTION OVERHAUL

Production quality has been a priority for Dr. Reinhardt and his management team since the acquisition of Chiron Corp. by Novartis in April 2006. Quality lapses at facilities in Liverpool, England, producing flu vaccine had triggered an enforcement action by regulatory authorities and crippled production in the two years preceding the takeover. The division s USD 1 billion investment program over five years spans production sites for flu as well other vaccines.

Construction of a completely new production plant is under way and is the final step in the remediation program at the Liverpool site. We will focus our egg-based flu vaccine production in Liverpool once the new facility is online, probably in time for the 2010-2011 flu season, Dr. Reinhardt says. The new Liverpool facility will have higher capacity than the division s three existing flu vaccine plants put together.

Meanwhile, the plant in Rosia, Italy, has been upgraded in preparation for the launch of *Menveo*, a EUR 40 million investment program. Vaccines and Diagnostics owns the world s first production plant for influenza vaccines based on a revolutionary new cell- culture technology. The plant located in

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Marburg, Germany, and representing a EUR 80 million investment will use modern biotechnology rather than the chicken eggs traditionally used for primary production of influenza vaccines.

Egg-based production requires a lead time of several months for ordering and receiving eggs, which can hinder response to unanticipated demands such as a pandemic, or worldwide outbreak of influenza, caused by the emergence of a new viral strain that is easily transmitted among humans. A second flu cell-culture plant is under construction in the United States, in Holly Springs, North Carolina. The Novartis investment there is expected to exceed at least USD 600 million partly supported by grants from the United States government.

In 2008, a new cycle of expansion began at the Marburg site as Novartis broke ground for a new production facility for rabies and tick-borne encephalitis vaccines in response to increased demand in recent years, as well as for a new building for quality control. The EUR 145 million project is scheduled for completion by the end of 2010 with regulatory approvals and commissioning expected the following year.

INFLUENZA: CORE FRANCHISE

Influenza vaccines are a core franchise at Vaccines and Diagnostics and production for the 2008-2009 season reached almost 70 million doses, unchanged from the previous year but 30% above the level of deliveries in the 2006-2007 flu season. The current flu season has been mild, however, and oversupply of flu vaccine in the United States as well as some European countries sharpened competition and intensified pressure on prices.

In addition to output of seasonal flu vaccine, Novartis is working closely with government and regulatory officials worldwide to support pandemic preparedness efforts. In 2007, Novartis received European Union approval for a mock-up application for *Focetria*, a new vaccine designed for use after the declaration of an influenza pandemic.

Focetria will be manufactured to contain the influenza strain declared at the time of a pandemic by the World Health Organization (WHO). The vaccine will include *MF59*, a proprietary adjuvant, or substance that boosts the immune response to a vaccine. Use of *MF59* could extend the vaccine supply by allowing for smaller amounts of active ingredients, known as antigens, to be used in each dose of the pandemic vaccine compared to vaccines without this additive.

In 2008 Novartis delivered supplies of a prepandemic vaccine to the US government, adding to the strategic stockpile being built in accordance with the US Pandemic Preparedness Plan. The vaccine is based on the H5N1 influenza strain, a potential pandemic virus that has circulated in birds across Asia since the original outbreak of avian flu in Hong Kong in 1999. Since 2003, there have been more than 350 confirmed cases of avian flu in humans but, according to the WHO, there is no evidence yet of sustained human-to-human transmission, a precondition for a pandemic outbreak.

Novartis withdrew its application for a centralized marketing authorization application (MAA) for *Aflunov*, another prepandemic vaccine, when the request by the European Medicines Agency for additional data could not be met within the applicable regulatory timeframe. Further clinical trials are under way after which the MAA will be re-submitted.

Clinical studies have shown that *Aflunov* is protective against the H5N1 strain and offers a degree of protection against other related influenza substrains. *Aflunov* also contains the *MF59* adjuvant that helps strengthen the immune response to the disease. A clinical study published in 2008 underscored the potential benefit of a pre-pandemic vaccine by showing that people immunized six years earlier with a vaccine based on an H5N3 influenza strain and containing *MF59* mounted a protective immune response after a single injection with *Aflunov*. The immune response was broadly cross-protective, covering all variants of H5N1 known to date.

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SANDOZ OVERVIEW

KEY FIGURES **(In USD millions, unless indicated otherwise)**	**2008**	**2007**
Net sales	**7 557**	7 169
Operating income	**1 084**	1 039
Return on net sales (%)	**14.3**	14.5
Research & Development	**667**	563
As a % of net sales	**8.8**	7.9
Free cash flow	**1 066**	1 112
Net operating assets	**13 948**	14 664
Additions to property, plant & equipment(1)	**422**	627
Number of associates (FTE)(2) at year-end	**23 146**	23 087

(1)Excluding impact of business combinations

(2)Full-time equivalent positions at year-end

2008 NET SALES ESTABLISHED VS. EMERGING/UNTAPPED MARKETS (in %)

(1)2008 Sandoz retail business net sales growth in US dollars vs. 2007

NEWS IN 2008

Overall improving performance as Sandoz, a world leader in generic pharmaceuticals, builds up global product portfolio and expertise in difficult-to-make generics. Active in 130 countries covering 90% of world s population. Strong presence in many established countries, while growing rapidly in emerging markets.

Net sales up 5% (+1% in local currencies) to USD 7.6 billion. Improving performance in many markets led by 13% lc growth in Central and Eastern Europe and leading position in Russia largely offset by a 10% decline in the United States from lack of new product launches in 2008.

Operating income rises 4% to USD 1.1 billion thanks to overall business expansion and productivity gains despite reduced contributions from the United States. Investments made in difficult-to-make generics and expansion in emerging markets. Operating margin falls slightly to 14.3% of net sales from 14.5% in 2007.

Emerging and untapped generics markets account for 36% of Sandoz net sales, rising 16% in 2008. Russia ranks as the third- largest Sandoz market, while other markets with low generic utilization rates particularly Japan and some European countries are targeted for expansion.

Difficult-to-make generics provide competitive advantage as more than 25% of 2008 net sales come from these higher-value products. Sandoz pioneering the development of biosimilars (generic versions of approved biotechnology drugs). *Binocrit* (biosimilar epoetin alfa) gains market share in Germany and drives 35% lc growth in Biopharmaceuticals.

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SANDOZ

Sandoz, the generic pharmaceuticals Division of Novartis, is the pioneer in difficult-to-make products that require specialized technologies, complex formulations such as patches or implants, or complex active pharmaceutical ingredients. Vertical integration in-house production from active ingredient to final dosage form has made Sandoz a global leader in anti-infectives as well as biosimilars, follow-on versions of existing biologic medicines that have lost patent protection. Now Sandoz is expanding this vertical-integration strategy to other therapeutic areas to reinforce its leadership in difficult-to-make generics.

Sandoz, the generic pharmaceuticals Division of Novartis, launched the first generic version of the blockbuster antibiotic Augmentin® in the United States in 2003.

Six years later, amoxicillin clavulanate potassium,the generic nameforAugmentin®, remains one of the best-selling products in the Sandoz portfolio. It is a success story in which Sandoz used its specialized technical expertise to create a difficult-to-make product.

Generics are high-quality, cost-effective copies that compete with originator medicines after the patent expires. The availability of generics frees up money for payors to reinvest in new innovative breakthroughs, says Andreas Rummelt, Ph.D., Group Head of Quality Assurance and Technical Operations and member of the Executive Committee of Novartis, who headed Sandoz until December 1, 2008. It s a fundamental trend in healthcare systems around the world.

Sandoz is leading the way in difficult-to-make generics. These are products based on challenging active pharmaceutical ingredients (API) or that require specialized formulations and technologies, ranging from implants and transdermal patches to extended- release tablets or inhalation devices. It is the centerpiece of our strategy, Dr. Rummelt says. Difficult-to-make products already contribute more than 25% of our net sales.

API development and production is an essential platform underpinning the difficult-to-make strategy. Antibiotics are the prototype of this strategy: the Anti-Infectives Business Unit at Sandoz develops and produces APIs used to produce tablets, vials and other formulations known collectively as final-dosage forms.

A proprietary API can secure patent protection, eventually translating into a competitive advantage toward other generic manufacturers. Moreover, in-house API production anchors the supply chain, improving prospects of placing a Sandoz generic in the market on Day One following patent expiration of the originator medicine.

Just as in the case of amoxicillin clavulanate, in-house API played a crucial role in the success of cefdinir, one of the most widely prescribed cephalosporin antibiotics in the United States; Sandoz beat rivals to market and reaped a commercial windfall in 2007.

In turn, vertical integration has been a catalyst for the aggressive push by Sandoz into biosimilars, follow-on versions of existing biologic medicines whose patents have expired. Sandoz is a pioneer in biosimilars. It brought the world s first two biosimilar products to market in the European Union and marketed the first biosimilar in the United States as well. The biotechnology platform we have established in anti-infectives is the foundation for success in biosimilars, says Ernst Meijnders, Head of the Anti-Infectives Business Unit. Once biotechnology capabilities are in place, they can be leveraged in more novel areas.

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Apart from anti-infectives, however, Sandoz has developed proprietary APIs for only about 10% of its products. That clearly isn t sufficient and we are making major investments to build the development capabilities for active pharmaceutical ingredients in other therapeutic classes, Dr. Rummelt adds.

CONTINUOUS IMPROVEMENT

Augmentin® posted net sales of more than USD 2 billion in the year before its main US patents expired, making the medicine a lucrative target for generic companies. Yet daunting technical hurdles deterred many potential generic rivals from entering the market. Augmentin® is a combination of clavulanic acid and amoxicillin, a penicillin- like antibiotic. The addition of clavulanic acid enhances the effectiveness of the antibiotic against many bacteria ordinarily resistant to amoxicillin.

Production of clavulanic acid requires both fermentation and chemistry, Mr. Meijnders says. It was considered a difficult product, and no other companies were able to develop it on a large scale.

Sandoz and Lek Pharmaceuticals, the Slovenian group acquired by Sandoz in 2002, had developed parallel processes for amoxicill in clavulanate API, and optimization of production has continued since the launch of the Sandoz generic. Continuous improvement extends to downstream operations and development of additional formulations.

We have a range of formulations for adults and children, including tablets, extended release forms, capsules and vials, Mr. Meijnders adds.

The Sandoz site in Kundl, Austria, is the hub of anti-infective operations. Production of penicillin began here shortly after World War II and decades of experience have forged a powerful biotechnology platform. Biotechnology and antibiotics are one of those rare occasions where a technology platform and a therapeutic area are a perfect fit, says Mr. Meijnders, who also serves as Head of the Kundl site.

By the time of the amoxicillin clavunalate launch, however, competition in generic antibiotics had begun to thin out, reflecting the special requirements of antibiotics production. Today Sandoz is the only developer and producer of antibiotics in Western Europe or the United States; most competitors are based in low-cost countries in Asia. Very few pharmaceutical companies have continued in the antibiotics business, Mr. Meijnders says.

Complexity of operations is one challenge. Production volume for some APIs produced in custom-built manufacturing plants ranges from tons to thousands of tons per year. You need dedicated facilities and dedicated sites to ensure that no cross- contamination can occur, Mr. Meijnders concludes.

Major pharmaceutical companies aren t necessarily interested in the upkeep and reinvestment required to handle penicillins and cephalosporins as their patents run out. That provides us with supply opportunities.

CENTERS OF EXCELLENCE

In 2007, Mr. Meijnders was tapped to lead a task force reviewing possibilities to expand development of new APIs in therapeutic areas outside anti-infectives. The initiative led to the creation of a separate unit for selection, development and production of APIs used in conventional generic medicines. To lead this new API unit, Sandoz selected Hansjuerg Wetter, Ph.D., former Head of Chemical Operations at the Novartis Pharmaceuticals Division.

Traditionally, generic companies have purchased APIs from outside suppliers and focused their development efforts on final-dosage forms. Hexal AG and its US-based affiliate Eon Labs Inc. the generic high- fliers acquired by Sandoz in 2005 bypassed API development and put only final-dosage forms on the market. By contrast, Lek was a completely integrated company, with development and production of both API and final-dosage forms.

Development activities at the new API unit will focus on a selective portion of the early Sandoz pipeline for which internal development and production could be translated into a competitive advantage, especially for difficult-to-make generics.

We can find suppliers for commodity- type APIs, Dr. Wetter says. We want to focus our efforts on situations where it s doubtful a competitor would supply us; where we have identified a proprietary technology we prefer to keep to ourselves, or where doing so would lead to early market access.

The new unit has set ambitious targets. A project team has identified 40 promising API development candidates and Sandoz aims to have 50 new APIs in development by 2010.

We also are introducing production of starting products for the Pharmaceuticals Division that previously were purchased externally, Dr. Wetter adds. Activities at Sandoz and the Pharmaceuticals Division overlap in other areas as well. Sandoz is making a major push in respiratory medicines and, at the same time, the Pharmaceuticals Division has innovative treatments for asthma and chronic obstructive pulmonary disease in advanced stages of clinical development.

The purely technical issues regarding particle properties of APIs and delivery systems are the same on both sides, and we are all participating in discussions on the development of these inhalation products, Dr. Wetter says.

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BROADEST BIOSIMILAR PROGRAM

Biosimilars are the epitome of difficult-to-make, follow-on products, and Sandoz has more than 25 years of experience in development and production of biologics. Sandoz co-developed and manufactured interferon alpha in Kundl in the 1980s, and has remained one of the world s biggest development and production sites for biologics. Though Sandoz manufactures more than a dozen recombinant proteins on behalf of other companies, that pedigree is not well- known because of confidentiality agreements with customers.

Omnitrope, a biosimilar human-growth hormone, was approved in 2006 by the European Medicines Agency, the main regulatory agency of the European Union, and the US Food and Drug Administration for long-term treatment of pediatric patients who have growth failure, and long-term replacement therapy in adults with growth- hormone deficiency.

In 2008, Sandoz introduced the new *Omnitrope* Pen with a liquid cartridge, providing increased treatment flexibility for physicians and a more convenient dosage form for patients. *Omnitrope* products also offer significant savings compared to the reference product Genotropin® and other recombinant growth hormones.

Epoetin Alfa HEXAL/Binocrit, the first biosimilar epoetin alfa, was approved by the European Union in August 2007.

Additional refinements of the products are in the offing. We have initiated more than 20 clinical studies with *Omnitrope* and *Binocrit*, says Hannes Teissl, Head of the Sandoz Biopharmaceuticals Business Unit. The Sandoz development program for biosimilars includes more than 25 projects, one of the broadest programs in the industry. We have production and development capacity in place, and we have shown that we are able to launch biosimilars, Mr. Teissl says. We are not just talking. We ve proven it.

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CONSUMER HEALTH OVERVIEW

KEY FIGURES CONTINUING OPERATIONS(1) (In USD millions, unless indicated otherwise)	2008	2007
Net sales	**5 812**	5 426
Operating income(2)	**1 048**	812
Return on net sales (%)	**18.0**	15.0
Research & Development	**313**	301
As a % of net sales	**5.4**	5.5
Free cash flow	**995**	772
Net operating assets	**3 179**	3 154
Additions to property, plant & equipment(3)	**160**	209
Number of associates (FTE)(4) at year-end	**13 014**	13 956

(1)Excluding discontinued Consumer Health operations divested during 2007

(2)2007 results include an exceptional USD 97 million of restructuring charges for the Forward productivity initiative

(3)Excluding impact of business combinations

(4)Full-time equivalent positions at year-end

2008 CONSUMER HEALTH MARKET INFORMATION

	OTC	Animal Health	CIBA Vision
Novartis net sales in USD billions	3.0	1.1	1.7
Novartis sales growth (lc)(1)	3%	3%	7%
Market segment growth(2)	3%	2%	4%
Novartis market share(2)	3.5%	6.0%	20.9%
Global industry rank(3)	4	6	2

(1) 2008 local currency growth vs. prior year

(2) Sources (OTC: Nicholas Hall; Animal Health: Internal analysis; CIBA Vision: Nielsen, GfK)

(3) Sources: Nicholas Hall, Vetnosis, Internal analysis

NEWS IN 2008

Consumer-driven businesses OTC (Over-the-Counter), Animal Health and CIBA Vision provide trusted and differentiated products to enable healthy lifestyle choices. Sustained Research and Development investments and geographic expansion are strengthening globally competitive positions.

Net sales grow 7% (+4% in local currencies) to USD 5.8 billion, led by the turnaround in CIBA Vision. Sharp rise in operating income, up 29% to USD 1.0 billion, comes from the strong business expansion and productivity gains from the Forward initiative. Operating margin in 2008 improves 3.0 percentage points to 18.0% of net sales.

OTC delivers above-market growth in many markets particularly in high-priority emerging markets thanks to expanding presence of strategic brands. Decline in the United States reflects changes in consumer spending that have affected this industry.

Animal Health, ranked number six in its industry, expands companion-animal business through product innovation and focus on key countries. Global farming crisis hampers growth of products for farm animals.

CIBA Vision benefits from launches of new contact lens products in the United States and other key markets, overcoming supply challenges in 2007 and strengthening its number two industry ranking. New product launches include both daily disposable lenses as well as weekly/monthly disposable lenses.

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CONSUMER HEALTH

Development of parallel, over-the-counter (OTC) versions of prescription-only medicines has been a driving force in robust growth of the OTC Business Unit at Novartis. The blockbuster prescription painkiller *Voltaren* was the prototype of prescription-to-OTC switches. Dynamic growth of *Voltaren* as an OTC brand as well as a prescription medicine underscores the positive synergy that can help sustain product franchises past patent expiry.

During the late 1990s, as basic patents on the Novartis painkiller *Voltaren* began to expire in countries around the world, the blockbuster prescription medicine embarked on a new, parallel path as a self-medication brand.

The additional approval of *Voltaren* as an over-the-counter (OTC) product underscored the strong commitment of Novartis to one of the most dynamic segments of the healthcare industry. OTC products can be purchased without a doctor s prescription at pharmacies or other retail outlets, and that ready availability enhances access to a familiar medicine such as *Voltaren*.

Increasingly, knowledgeable consumers rely on OTC products to medicate common ailments and make healthy lifestyle choices. Moreover, because OTC products are not usually entitled to reimbursement, self-medication allows payors to conserve scarce funds for prevention and treatment of more serious diseases.

OTC products are familiar in North America and Western Europe, but self-medication is less well-established in parts of Asia, including Japan, and in many emerging markets. Therefore, the OTC Business Unit at Novartis is focusing on geographic expansion as well as innovation to accelerate growth.

Novartis currently ranks fourth globally by sales among OTC manufacturers, but has been the fastest-growing company among the top five, posting compound annual average growth of 12.5% since 2003. Seven Novartis OTC brands have worldwide sales of more than USD 100 million, but OTC-switch brands have been the driving force behind the strong growth of recent years. Along with *Voltaren*, Novartis has developed and introduced OTC versions of the anti-fungal medicine *Lamisil* and of the *Nicotinell* smoking-cessation patches.

The next major switch from prescription to OTC will involve a blockbuster medicine that originated outside Novartis laboratories. In 2005 Novartis acquired rights to switch and commercialize Prevacid®, a prescription-only (Rx) medicine in different dosage forms currently used to treat a number of gastric acid-related disorders, including heartburn. Limited to the United States, the agreement gives Novartis the rights for product development, design and conduct of clinical studies and regulatory submissions to the US Food and Drug Administration (FDA) for a prescription-to-OTC switch of the Prevacid® products.

Preparations in support of the biggest launch in recent years by the OTC Business Unit continue on schedule. Over-the-counter Prevacid® is expected to become the second-biggest OTC brand after *Voltaren* based on projected sales, says Larry Allgaier, Global Head of the OTC Business Unit. The total number of prescriptions written for prescription-only Prevacid® in the last decade has surpassed all other heartburn brands.

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IDEAL CANDIDATE

The most promising switch candidates are medicines with strong records of safety and efficacy in indications that can be self- diagnosed and treated effectively and safely by consumers. *Voltaren* qualified on all counts.

The Pharmaceuticals Division of Novartis already had developed *Voltaren Emulgel*, a convenient topical gel formulation. *Voltaren Emulgel* is effective and safe, says Barry Cohen, Vice President and General Manager, Global Pain Category, at the OTC Business Unit. It was an ideal product to make more accessible to patients to treat their backache, shoulder, neck and joint pain, and other muscle aches and pains. Consumers usually don t go to the doctor to treat these types of pains. Unless it s really bad, they typically go right to the pharmacy for an OTC remedy.

The OTC version of *Voltaren Emulgel* was first launched in Italy and Germany, and broader access made the product even more successful. It is now available over- the-counter in more than 40 countries and since 2000 the *Voltaren* OTC franchise has posted a compound annual growth rate of more than 15%.

Prescription *Voltaren Emulgel* has remained on the market in many countries and continues to grow, underscoring the positive synergy between prescription-only and OTC medicines. People expected that switching *Voltaren Emulgel* would cause sales of the prescription products to decline, but promotion of the OTC version to consumers has actually helped sustain the prescription franchise long past the point of patent expiry, says Carl Ward, Global Vice President of New Growth Opportunities and OTC Switches at the OTC Business Unit. Clearly, the brand and medical heritage of prescription *Voltaren* is a critical part of what makes pharmacists willing to recommend the OTC product.

BROADENING THE FRANCHISE

A steady stream of new formulations is another key reason for the success of OTC *Voltaren*. For all the success of the topical gel, a non-prescription tablet formulation was essential to make *Voltaren* a leading global brand. In the OTC analgesic category, the market for tablets is three times as large as topical analgesics, and the bulk of the prescription *Voltaren* business is tablets, Mr. Cohen says.

OTC products normally are less potent and approved for different indications than the original prescription versions. For example, as a prescription tablet the antifungal *Lamisil* is used to treat infections of fingernails or toenails. OTC *Lamisil*, however, is used at lower doses in a topical form to treat athlete s foot. *Nicotinell* smoking-cessation patches prescribed by physicians come in strengths matched to nicotine intake of heavy smokers; OTC versions of the patch are used by people who smoke fewer than 20 cigarettes per day.

The initial tablet formulation of OTC *Voltaren* was 12.5 milligrams (mg), half the lowest dose of prescription *Voltaren* tablets. The 12.5-mg tablet was a good way to enter the tablet segment and gave us some uplift, but it wasn t driving the type of results we were looking for, Mr. Cohen acknowledges. So we started working with the Pharmaceuticals Division to determine how we could best switch the 25-mg prescription dose to OTC status.

In 2006 regulatory authorities in Italy approved the 25-mg *Voltaren* tablet as an OTC product and regulators in Germany followed suit the next year. Sales of the new OTC 25-mg tablet have climbed rapidly in both markets. It s got the trusted *Voltaren* name and what pharmacists view to be a highly efficacious, but safe, dose, Mr. Cohen adds. We are aggressively pursuing regulatory submissions for the OTC 25-mg dose in other countries. And we have case studies showing that our continued support of the OTC tablets is helping sales of prescription- only *Voltaren* tablets, as well. It s really a win-win.

Voltaren now is the fourth-largest OTC analgesic worldwide and the fastest-growing among the top 10 global OTC analgesic brands. We ve achieved that despite the fact that we are mainly a topical franchise while the majority of consumers around the world use primarily systemics, Mr. Cohen says. And OTC *Voltaren* still isn t available in the world s two biggest self- medication markets for topical analgesics, the United States and Japan.

The OTC franchise has preserved the *Voltaren* brand heritage focusing on body pain and the ability of *Voltaren* to restore mobility as well as relieving pain. *Voltaren* is the body- pain medicine, Mr. Cohen says. That s how doctors and pharmacists know it.

A new product launched in 2008 perpetuated the *Voltaren* heritage while extending the OTC franchise in new directions. Novartis launched *Volta flex* in several countries, including Germany and Switzerland. *Voltaflex* includes the dietary supplement glucosamine, which helps provide relief from the pain caused by osteoarthritis and may help slow down the evolution of the disease. The message to consumers is that *Voltaflex* helps to restore flexibility and thus helps with mobility. That s the ultimate benefit to the consumer: Even if you have arthritis you can get out and be active walk and play golf or tennis, Mr. Cohen says.

JAPAN AND THE UNITED STATES

Markets in Asia use fewer OTC medications than developed countries in the West. Growth of Japan s OTC market has been anemic in recent years, but switches of three medicines since 2003 have enabled Novartis to outgrow the market and gain market share. Those successful switches

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have galvanized a radical shift in strategy in which Novartis is bucking conventional wisdom and establishing independent OTC sales and marketing, as well as research and development functions, in Japan. By comparison, the OTC operations of virtually all other international companies are joint ventures with local partners.

Japan is an extremely important market, and working at arm s length with local partners hasn t been as successful as we would have liked, says Charlie Hough, OTC Region Head Asia Middle East and Africa. We are committed to investing here and building our own business, gaining a foothold in the market and making things happen quickly.

Since ending the most recent partnership, Novartis has won approval for two prescription-to-OTC switches: *Nicotinell* nicotine replacement patches and *Zaditen*, an antiallergy and antiasthma drug widely used by patients and physicians in Japan.

Ultimately, pursuing the partnership approach would limit the potential of our brands, Mr. Allgaier says. With *Lamisil*, *Zaditen*, *Nicotinell* and now *Voltaren* coming, we have a responsibility to grow these Novartis assets and to optimize their potential, both for self-care of Japanese consumers and financially for Novartis.

For almost a decade, *Nicotinell* has been the only prescription patch approved by Japanese authorities for nicotine- replacement therapy. It was the only nicotine patch that consumers and pharmacists were even aware of, Mr. Hough says.

The proportion of smokers in Japan remains high: 53% of adult men and 13% of adult women smoke. The Japanese government raised tobacco taxes in 2006, and another increase is expected in 2009.

Along with the 2006 tobacco-tax hike, the government agreed to reimburse most of the cost of *Nicotinell* treatment in a move intended to encourage smokers to quit. It s very unusual in Japan for the government to proactively decide to reimburse a prescription product that hadn t been funded previously. Typically, decisions go in the reverse direction, Mr. Hough says.

Novartis had filed regulatory applications in 2005, seeking approval to launch lower-dose OTC versions of *Nicotinell* patches. Following a protracted review, the government approved that application in June 2008 along with similar applications from two other international pharmaceutical companies. Novartis launched OTC *Nicotinell* patches six weeks ahead of competitors and gained market leadership. We still have the prescription *Nicotinell* patches on the market as well. We re competing in both markets, Mr. Hough says.

OTC *Nicotinell* patches are differentiated from prescription patches by dosage. The strongest prescription patch targets people who need a doctor s intervention because they may be heavier smokers or have smoked for a very long time. By contrast, the OTC *Nicotinell* patch is suitable for people ready to quit smoking without a doctor s guidance.

To emphasize the role of pharmacists in correct use of the OTC *Nicotinell* patch, Novartis has held more than 100 educational sessions with pharmacists around Japan. We tell pharmacists that when someone walks in and wants to quit smoking, they should be cautious about recommending the OTC patch unless they are convinced that the person can quit without a doctor s intervention and guidance, Mr. Hough says. Someone smoking 30 to 40 cigarettes a day for the past 20 years should probably see a doctor and start with the prescription *Nicotinell* program. There would be too great a drop in nicotine intake with the OTC patch, and less likelihood to get the full benefit of nicotine-replacement therapy.

OTC *Zaditen* was launched in late 2007 as an allergy product, available as eye drops and a nasal-spray formulation as well as capsules. Strong sales during the peak 2008 allergy season catapulted *Zaditen* to Japan s third-largest OTC allergy product. It s not that easy to jump in with a new OTC brand against some pretty strong competitors, Mr. Hough says. A lot of the success of *Zaditen* is because of the prescription halo. With *Nicotinell* but particularly with *Zaditen* when our sales force visits a pharmacy and begins talking about our brands, there already is high awareness and a lot of credibility.

Voltaren also has a strong position as a prescription medicine in Japan and is an obvious candidate among the pipeline of potential switch products. With *Voltaren*, we would start with extremely high awareness in Japan, and a positive image with both physicians and consumers, Mr. Hough adds. That helps us jump right out of the gate.

In the United States, the OTC Business Unit submitted a regulatory application two years ago seeking FDA approval of OTC *Voltaren* gel. The application included results from clinical trials involving more than 900 patients with osteoarthritis in a hand or knee. In two efficacy studies and a 12-month safety study, *Voltaren* Gel significantly reduced pain from hand and knee osteoarthritis and that pain relief was sustained through the end of treatment.

During late 2007 the FDA approved *Voltaren* Gel 1%, though as a prescription- only treatment for pain associated with osteoarthritis. It was the first topical prescription treatment approved by the FDA for the indication and the first new medication approved in the United States for treatment of osteoarthritis since 2001.

In March of 2008 Novartis licensed US marketing and distribution rights to *Voltaren* Gel to Endo Pharmaceuticals Inc., a company specializing in prescription pain products. Under the agreement, Novartis received an upfront cash payment of USD 85 million, retains the OTC-switch rights and will receive royalties on net sales of *Voltaren* Gel in the United States. As experts in prescription pain medication, Endo will help us build the *Voltaren* brand in the US, Mr. Ward says.

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CORPORATE CITIZENSHIP

Corporate Citizenship at Novartis is an integral part of how we operate and a key to our success.

Our Corporate Citizenship commitment rests on four pillars:

Patients

Novartis seeks to ease suffering and enhance the quality of life for patients, including those who cannot afford treatment.

People and Communities

We strive to provide our associates with the safest possible workplaces, and to promote their health and well-being. We are an integral part of the communities that host our operations.

Environment

Careful stewardship of natural resources, particularly tight control of waste, greenhouse-gas emissions, and energy efficiency is important to Novartis.

Business conduct

We strive for high performance with integrity.

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CORPORATE CITIZENSHIP KEY PERFORMANCE INDICATORS

Indicator(1)	2008	2007	2006	2005	2004
Economic(2)					
Net sales in USD billions	**41.5**	38.1	34.4	29.4	25.7
Net income in USD billions (% of net sales)	**8.2 (20)**	6.5 (17)	6.8 (20)	5.8 (20)	5.4 (21)
Research & Development in USD billions (% of net sales)	**7.2 (17)**	6.4 (17)	5.3 (15)	4.8 (16)	4 (16)
Purchased goods and services(3) in USD billions (% of net sales)	**20.3 (49)**	19.4 (51)	15.8 (46)	13.3 (45)	11.2 (44)
Personnel costs in USD billions (% of net sales)	**10.6 (25)**	9.9 (26)	8.7 (25)	7.5 (25)	6.5 (25)
Taxes in USD billions (% of income before taxes)	**1.3 (14)**	0.9 (13)	1.2 (15)	1.0 (14)	1.0 (16)
Dividends in USD billions (% of net income)	**4.3 (53)**	3.3 (51)	2.6 (38)	2.0 (35)	2.1 (39)
Cash returned to shareholders via share repurchases in USD billions (% of Group total net income)	**0.3 (0)**	4.7 (39)	0 (0)	0.5 (8)	1.7 (32)
Share price at year-end (CHF)	**52.70**	62.10	70.25	69.05	57.30
Patients					
Access to medicine(4): value in USD millions	**1 259**	937	755	696	570
Access to medicine(4): number of patients reached [million]	**74**	65.7	33.6	6.5	4.25
People and Communities					
Number of full-time equivalent positions	**96 717**	98 200	100 735	90 924	81 392
Resignations (incl. retirements), separations, hiring (% of associates)	**-10, -5, 14**	9, 4, 17	8, 4, 19	8, 4, 16	7, 3, 15
Women in management(5)(% of management)	**37**	35	31	28	
Lost-time injury and illness rate (LTIR)(7) [per 200 000 hours worked](2)	**0.34**	0.42	0.45	0.51	0.47
Total recordable case rate (TRCR)(6) [per 200 000 hours worked](2)	**1.08**	1.41	1.43	1.34	0.99
Transportation-related injuries leading to lost time	**77**	92			
ISO/OHSAS or EMAS certification (as % of production)	**59**	63	63		
Environment(2),(8)					
Water use (excludes cooling water) [million m(3)]	**15.0**	15.4	15.2	15.0	14.4
Energy [million GJ]	**16.9**	16.7	16.4	15.3	13.8
Emission CO2/GHG, Scope 1: Combustion and processes [1000 t]	**404**	408	408	383	372
Emission into air: halogenated and nonhalogenated VOCs [t]	**1 818**	1 892	2 021	1 979	1 316
Total operational waste not recycled [1000 t], hazardous and non-hazardous	**154**	177	156	115	97
Ethical Business Conduct					
Number of associates trained in 2008 on Code of Conduct (e-learning courses)(9)	**15 990**	16 697	14 574	33 000	
Managers completing certification on Code of Conduct	**26 750**	27 000	23 000	20 000	
Cases of misconduct reported/substantiated(10)	**884/231**	906/390	651/320	442(11)/240(11)	7(12)/7(12)
Dismissals/resignations (related to misconduct)(10)	**162**	221	153	131(11)	7(12)
Number of suppliers	**228 769**	228 558			
Number of suppliers informed of Novartis Third-Party Guidelines (Annual sales of more than USD 10 000)	**28 792**	61 715	42 200	39 000	30 000
Number of suppliers to confirm key standards(13) (self-declaration)	**1 157**	1 377	8 600	5500	4600

(1) Data reported in the Ethical Business Conduct (except Number of suppliers items) and Health, Safety & Environment sections (except Lost-time injury and illness rate) include the entire Group; Data reported in Number of suppliers items excludes the Vaccines and Diagnostics Division
(2) All items relate to continuing operations, unless stated otherwise
(3) As included in the Group s Value Added Statement
(4) See table on page 72 (Access-to-medicine table)
(5) Management defined locally; the actual reporting relationship of these executives is to executives and/or the boards of directors within the companies that employ them
(6) Includes all work-related injury and illness, whether leading to lost time or not
(7) Excludes data for contractors
(8) Details see: www.novartis.com/hse
(9) 2008 figure includes new associates and other associates not previously trained
(10) Figures of previous years have been updated to reflect completion of outstanding investigation
(11) From April to December 2005
(12) From October 2003 to September 2004
(13) In 2007 Novartis modified financial requirements for self-declarations by suppliers, focusing on suppliers with the highest business volumes and resulting in a significant decline in the number confirming key standards

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NEWS IN 2008

OVERVIEW	Corporate Citizenship at Novartis rests on four pillars: Commitments to Patients, to People and Communities, to the Environment and to Ethical Business Conduct.
PATIENTS	Treatments worth USD 1.26 billion are contributed through access-to-medicine programs in 2008, reaching 74 million patients in need.
	In April 2008, Novartis announces a 20% average reduction in the price of *Coartem* tablets made possible through efficiency gains in production at state-of-the-art facilities in China and the United States.
	In December 2008, Swiss health authorities approve a new pediatric formulation of *Coartem* that will enhance taste and convenience for young children who are especially vulnerable to malaria. The dispersible formulation is a joint development by Novartis and Medicines for Malaria Venture, a nonprofit foundation dedicated to the development of affordable new antimalarials.
PEOPLE AND COMMUNITIES	In Brazil, the local Novartis organization adds more than 80 disabled people to its payroll, in line with national legislation to step up recruitment of people with disabilities; more than 20% of the new disabled employees at Novartis are sales representatives, calling on healthcare professionals.
ENVIRONMENT	Novartis issues Energy Excellence guidelines for buildings and equipment worldwide, aiming to ensure efficient, cost-effective and climate-conscious use of energy.
BUSINESS CONDUCT	The Novartis Pharmaceuticals Division updates and broadens its Business Practices Policy to set additional global standards for both promotional and non-promotional activities, such as interactions with healthcare professionals, patients and the donation of grants.
	Novartis again achieves top-level positions in influential rankings and is named healthcare super sector leader in the 2008 update of the Dow Jones Sustainability World Index; moves up five positions, to number 20, in the Barron s magazine list of the world s most respected companies; ranks number two among pharmaceutical companies in Fortune magazine s list of World s Most Admired Companies and is again included in the 2008 World s Most Ethical Companies list from Ethisphere Institute.
	Novartis also receives the China Charity Award, the country s highest honor, ranking number one in the category Most Caring Foreign-Invested Enterprise. The award, established by the Chinese Ministry of Civil Affairs, recognizes social responsibility programs at Novartis, especially immediate and sustained support of relief efforts in the wake of the earthquake that struck western China in May 2008.

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CORPORATE CITIZENSHIP

Corporate Citizenship at Novartis begins with our ability to innovate. The more successful we are at discovering, developing and marketing new medicines and vaccines, the greater benefit we can offer patients, healthcare professionals, associates, shareholders and other stakeholders. During 2008, medicines and vaccines from Novartis were used to treat and protect more than 850 million people around the world, according to internal estimates.

Innovation is the essence of our mission at Novartis: to discover and develop innovative products to prevent and cure diseases, to ease suffering and to enhance the quality of life.

Novartis has a proud legacy of pioneering discoveries to treat major diseases, from cancer and mental disorders to organ transplantation and cardiovascular disease. In 2008, Groupwide research and development expenditures climbed 12% to USD 7.2 billion, representing 17% of net sales. Novartis research labs rank among the most prolific in the healthcare industry: Between 2000 and 2008, the US Food and Drug Administration (FDA) approved more new medicines from Novartis than any other major pharmaceutical company.

During 2008, medicines and vaccines from Novartis were used to treat and protect more than 850 million people around the world, according to internal estimates. If all the patients reached by Novartis in 2008 stood shoulder-to-shoulder, the line would circle the earth 11 times.

The pharmaceutical industry has made major contributions toward improving both quality and length of life. According to estimates, more than 70 million people in the United States have high blood pressure and more than 300 000 Americans die each year from stroke, heart attack and heart failure associated with high blood pressure. More than 4 million Americans with high blood pressure were treated with *Diovan* in 2008. An external study showed that treament with *Diovan* is estimated to have prevented more than 60 000 strokes, heart attacks and cases of heart failure, avoiding more than USD 400 million in hospitalization costs that year.

While such gains are impressive, society faces enormous challenges due to aging populations, sedentary modern lifestyles and the explosive spread of chronic diseases, not only in developed nations of North America and Western Europe, but also in emerging countries on other continents.

A study of the economic burden of chronic disease from the Milken Institute, an independent economic think tank based in the United States, acknowledges that dramatic improvements in therapies and treatment have led to higher quality of life, less disability and lower rates of mortality.

The study s authors caution that, even as treatment outcomes and mortality have been improving, rates of chronic disease are steadily increasing and, if left to grow unchecked, threaten to cancel out gains. They add: Reducing the avoidable costs associated with these [chronic] conditions is central to meeting the twin challenges of promoting affordable healthcare and fostering continued economic growth.

Our purpose is to change the trajectory of some of these chronic diseases and their impact on individuals and society,

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says Daniel Vasella, M.D., Chairman and Chief Executive Officer of Novartis. The Milken Institute report underscores the enormous economic impact that innovation can have on society in addition to benefits for individual patients, Dr. Vasella adds.

INNOVATION: SCIENTIFIC MARATHON

Corporate Citizenship at Novartis begins with our ability to innovate. The more successful we are at discovering, developing and marketing new medicines and vaccines, the greater benefit we can offer patients, healthcare professionals, associates, shareholders and other stakeholders around the world.

Our commitment to innovation is not without risk. Only one out of 10 000 compounds synthesized in Novartis Group labs ever reaches the market. It can take years even decades to identify biological targets, unravel the roles they are believed to play in diseases and then synthesize a chemical compound or design a biologic therapy that inhibits or activates the target. That achievement is just the beginning. On average, another five years of preclinical testing is required before regulatory authorities allow the new medicine to be tested in humans, and subsequent clinical trials and registration eat up an additional seven years. The cost of that scientific marathon, on average, exceeds a billion dollars for each novel treatment that reaches the market.

At the Novartis Institutes for BioMedical Research (NIBR), scientific opportunity and unmet medical need are the prime criteria by which potential programs are judged. One measure of that strategy is that nine Novartis medicines have been designated as orphan products in Europe during the past five years. The orphan designation is a status reserved for medicines used to treat rare diseases, and entitles the manufacturer to a period of market exclusivity if development and testing are successful.

We do work on rare diseases, first and foremost to improve the lives of patients and their families, says Mark Fishman, M.D., President of NIBR and member of the Executive Committee of Novartis. But by no means do we study only rare diseases, he adds.

The observations we make in rare diseases often can be extrapolated to more common diseases. So we anticipate that almost all of these medicines will find a place in broader markets. (For other examples of NIBR s research strategy, see pages 35-36.)

Along with rare diseases, some of the world s biggest killers such as malaria, tuberculosis and dengue fever have often been overlooked because they afflict predominantly poor countries that lack funds to pay for modern medicines. To address the dilemma of these neglected diseases, Novartis in 2003 founded a pro bono research institute in Singapore in partnership with the city-state s Economic Development Board. The Novartis Institute for Tropical Diseases (NITD) is applying the most advanced techniques and tools of biomedical research to dengue fever, drug- resistant tuberculosis and malaria. Any therapies discovered at the institute will be made available to poor patients without profit.

In 2007, Novartis extended the NITD model to vaccines, creating the Novartis Vaccines Institute for Global Health (NVGH), based in Siena, Italy. NVGH is the first such institute with a nonprofit mission established by a major vaccine manufacturer. All vaccines developed by the institute will be provided at an affordable and accessible price to populations of developing countries. (For more about NVGH, see page 71.)

PATENTS SAVE LIVES

Patents are rights granted to anyone who invents a new product, a new process or a new use, such as a novel indication for a

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known medicine. Patent protection lasts at least 20 years from the date the patent application is filed, which is usually right after the molecule is discovered, at the beginning of the research process. That is the reason why patent life in the pharmaceutical industry is only 11 years, on average, because of the years of testing required to bring a new medicine from the laboratory to the pharmacy shelf.

For research-based organizations such as Novartis, patents and intellectual property systems are vital to our ability to continue developing innovative medicines in the future. Robust patent systems help patients by stimulating the long-term research and development efforts needed to create groundbreaking therapies.

Strong patent and other intellectual property rights are critical in the pharmaceutical industry, where developing medicines is a very high-risk endeavor. Indeed, weakening intellectual property protection in some countries represents a vexing dilemma to Novartis given our strategic focus on innovation.

Patents are the foundation for sustained investment in research and development, says Thomas Wellauer, Ph.D., Head of Corporate Affairs and member of the Executive Committee of Novartis. Novartis and other companies are spending billions of dollars every year but that money will dry up very quickly without any prospect of an economic return.

Some claim patents are in direct conflict with access to medicines. *Coartem*, the pioneering malaria treatment from Novartis, demonstrates that patents and access are not mutually exclusive. In partnership with the World Health Organization and other international organizations, Novartis provides *Coartem* for public-sector use in developing countries at no profit.

The *Coartem* program is an example of how public health emergencies can be effectively addressed through a collaborative approach among industry, governments and nongovernmental organizations. (For an update on the malaria program see page 73.)

HUMAN RIGHTS: LIVING UP TO COMMITMENTS

In December 2008, the United Nations marked the 60th anniversary of the Universal Declaration on Human Rights, the cornerstone of international human rights law. Novartis was one of the first companies to adopt a formal policy statement committing to support the protection of human rights, and our company has been publicly acknowledged by important stakeholders in this field as a leader in best practice.

Raising ethical business standards throughout our sphere of influence is a key principle of our commitment to the United Nations Global Compact, which asks companies to embrace, support and enact a set of core values in the areas of human rights, labor standards, the environment and efforts to combat corruption.

Human rights are essential elements of Corporate Citizenship, and responsibilities related to human rights have been integrated into corporate practices to ensure we live up to our commitments. Novartis has remained at the forefront of initiatives with special relevance to the pharmaceutical industry, ranging from access to medicine in the developing world to corporate activities that contribute to adequate standards of living and other economic, social and cultural rights.

Novartis was one of the first global enterprises to use the Human Rights Compliance Assessment, a tool for internal due diligence, in cooperation with the Danish Institute for Human Rights. The first pilot assessments examined Novartis operations in Turkey and Taiwan; a third assessment was conducted in South Africa in 2008 and the next assessment is scheduled for China in 2009. Testing the tool in various operational and cultural settings helped to adapt it to pharmaceutical-specific issues. It also increased awareness about human rights and triggered concrete measures, including more explicit policies regarding religious practices, improved infrastructure for associates with physical disabilities, and increased training about appropriate job interviews.

Novartis interacts with an increasingly complex map of stakeholders with diverse sometimes conflicting expectations. To navigate amid such contradictory demands, Corporate Citizenship is managed actively across countries and businesses and is ingrained in our commitments to patients, to people and communities, to the environment and to ethical business conduct.

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CORPORATE CITIZENSHIP: TARGETS AND RESULTS FOR 2008 AND TARGETS FOR 2009

UN Global Compact		
Targets 2008	**Results 2008**	**Targets 2009**
Publish a case study about Corporate Citizenship at Novartis. Continue to look for opportunities to support the United Nations Global Compact in shaping projects and opportunities for maximum impact.	Delivered a case study on developing new markets in rural India from a human rights perspective that will be included in a Harvard Business School publication. Supported the first UN Global Compact Leading Companies Retreat in Boston (US).	Participate in the Human Rights Working Group of the UN Global Compact to advance thinking on compliance assessments for human rights as well as concepts for access to medicine.
Respect for Human Rights		
Targets 2008	**Results 2008**	**Targets 2009**
Pilot a Human Rights Compliance Assessment in an additional country and develop a pharma specific version of the assessment. Support the Business Leadership Initiative on Human Rights (BLIHR) in development of an online tool to help companies assess and address challenges related to human rights. Contribute to the new round of discussions about business and the right to health.	Conducted the third full application of the tool at Novartis South Africa and supported the Danish Institute for Human Rights to test proposed elements of a pharma-specific version. Built part of the steering group to develop the prototype of the online BLIHR matrix, presented at the 60th anniversary of the Universal Declaration of Human Rights. Published article on corporate responsibilities for access to medicine in the Journal of Business Ethics.	Test the tool for assessing human rights compliance in a fourth country and continue to facilitate the development of a pharma-specific version by sharing the pioneering experience. Test the BLIHR Matrix tool for a cross-check of the company s main policies regarding the completeness in terms of human rights.
Transparent Reporting		
Targets 2008	**Results 2008**	**Targets 2009**
Release 2007 Communication on Progress. Continuously update the Citizenship@Novartis website.	Released the 2007 Communication on Progress reporting on the commitment of Novartis to the 10 principles of the UN Global Compact (UNGC). The Citizenship@Novartis website was regularly updated.	Release the 2008 Communication on Progress on the 10 principles of the UNGC. Continuously update Citizenship@Novartis.
Government Relations/Lobbying		
Targets 2008	**Results 2008**	**Targets 2009**
Publish additional position papers about healthcare topics to maintain transparency with topics of interest to external stakeholders.	Published new position papers on human rights and updates for Disclosure of Clinical Research Information. Expanded Public Affairs training in emerging markets. In 2008, Novartis spent USD 24 million in support of major international, US and pan-European trade associations.	Publish additional position papers about healthcare topics of interest to external stakeholders. Continue improving Public Affairs skills in all markets.
Financial Community		
Targets 2008	**Results 2008**	**Targets 2009**
Transition to the third generation guidelines (G3) for the 2007 Global Reporting Initiative (GRI) report.	Released Novartis GRI 2007 report using the enhanced G3 Sustainability Reporting Guidelines. GRI confirmed an A+ application level.	Release 2008 GRI report using G3 Guidelines and maintain ranking. Strive to maintain a top industry rating for corporate citizenship engagement.

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COMMITMENT TO PATIENTS

To make new medicines broadly available to patients as early as possible, Novartis is exploring a number of new pricing approaches, including money-back guarantees and other types of performance-based pricing. Novartis also emerged as an industry leader in early engagement with health authorities on health-economic evaluations that are becoming increasingly important in certain countries for patients access to new medicines.

Anna Cranz is a student majoring in psychology at a major European university.

For many years, higher education seemed an impossible dream for Ms. Cranz who suffers from severe asthma. Diagnosed after her first life-threatening attack at the age of only 18 months, her childhood was a series of dashes to hospitals for emergency treatment.

Asthma is a chronic disease in which inflammation causes bronchial tubes in the lungs to swell, narrowing airways and leading to wheezing and breathlessness. The inflammation results from diverse environmental triggers, called antigens. Growing up in the idyllic English countryside, Ms. Cranz battled antigens such as grass pollen and dust mites, while the damp climate further aggravated her condition.

Pets were taboo. I wasn t allowed to have any cuddly toys because of the risk of dust mites, she adds. My teddy bear had to spend the night in the freezer before I could play with it.

Ms. Cranz praises the care she received in Britain s National Health Service (NHS), but physicians were not able to stabilize her condition. She missed so much school that her grades suffered. I was the person who would come and visit the class rather than being part of it, she sighs. Teachers and doctors warned that the stress of an academic career would be dangerous. They told me not to think about going to university to just take it easy and try to breathe, she adds. I was devastated.

Then something changed in her life. I had turned 18 and was allowed to enroll in a clinical trial for *Xolair*, a new treatment for asthma from Novartis, Ms. Cranz recalls. The improvement was dramatic. I didn t really notice from the very first *Xolair* injection because I was on such high doses of existing medication. Then, slowly, over a period of about six months, I started reducing my medication.

The frequency of severe attacks declined from three to four per month to one or two per year. And I ve been attack-free for a full year, she adds. I can live a normal life. Obviously my asthma has to be controlled, but that s possible with *Xolair*. My life doesn t revolve completely around the disease anymore. It s no longer the dark star of my cosmos.

EXPLORING PRICING OPTIONS

Innovation is a precondition for a breakthrough medicine like *Xolair*. Bureaucratic obstacles, however, can delay or even prevent broad access for patients such as Ms. Cranz, as Novartis and other pharmaceutical companies negotiate pricing and reimbursement agreements. Governments, health authorities and other payors have to balance the desire to provide the best possible care to all citizens against limited funds.

To support payors in this dilemma and to make new medicines broadly available to patients and physicians as early as possible,

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Novartis is exploring a number of new arrangements, including money-back guarantees and other types of performance-based pricing. Moreover, Novartis has emerged as an industry leader in working with health authorities to ensure clinical trials are designed to generate data required for rapid health-economic evaluations.

Novartis is ready to try new things, says Jens Grueger, Ph.D., Head Pricing and Reimbursement at the Novartis Pharmaceuticals Division. We want to work together with payors and we welcome their best ideas as a starting point for discussions.

Because Novartis launched so many new products in recent years, it has had greater exposure to trends affecting market access than rival pharmaceutical companies. On one hand, we faced more varied issues than any other company, but we also have seen opportunities that no one else was able to see, Dr. Grueger adds.

To ensure access to *Xolair* for patients in the United Kingdom, Novartis offered Britain s Ministry of Health a pricing model that incorporates a money-back guarantee. In the approved-patient population people older than 12 with severe asthmatic asthma and presence of IgE antibodies confirmed by a diagnostic test *Xolair* has been shown to be cost-effective across several measures, in part by reducing other healthcare-associated costs such as fewer emergency-room visits and hospital admissions.

Not all severe asthma patients respond to treatment with *Xolair*, however, and it is difficult to predict responders on the basis of pretreatment demographic or clinical characteristics. After a hospital has entered in the agreement, it registers each patient initiated on *Xolair* treatment and, after 16 weeks, the outcome of that initial phase of treatment is assessed, Dr. Grueger says. If defined goals are not achieved, Novartis refunds the cost of the drug.

Another innovative medicine, *Lucentis*, is the only approved therapy that has demonstrated improvement in vision and vision-related function in patients with the wet form of age-related macular degeneration (AMD), the leading cause of blindness in people over 50. Loss of central vision severely affects quality of life for people with AMD due to increasing difficulty in performing normal daily activities such as reading, telling the time, recognizing faces or driving.

Lucentis has been approved in more than 70 countries. It also has received positive health-economic assessments from a number of countries, including the United Kingdom, Australia, Canada, the Netherlands and Sweden.

Britain s National Institute for Clinical Excellence (NICE), a government agency established to evaluate the cost-effectiveness of new medical treatments, also recommended *Lucentis* as a cost-effective therapy for people with wet AMD on the basis of a new reimbursement plan with Novartis. Under the agreement, the NHS will fund the first 14 injections in each affected eye, and Novartis will reimburse drug costs for any subsequent *Lucentis* injections. Additional dose-capping agreements have been introduced for *Lucentis* in Australia and Canada.

This is an important collaboration that will ensure patients living with wet AMD in England and Wales receive the best possible care, says Trevor Mundel, M.D., Head of Global Development at the Novartis Pharmaceuticals Division.

Efforts by Novartis to test new approaches to pricing reflect the rising influence of payors in decisions about use of medicines. In many countries, traditional prescribing autonomy of physicians is changing due to cost-containment measures, including use of formularies, or lists of preferred drugs. Similarly, decisions on reimbursement of new drugs are increasingly based on economic analysis in addition to the clinical performance of a new medicine.

Novartis believes the interests of patients, physicians, payors and providers can be aligned through pricing arrangements for which payment is directly related to the value created by our products. Where we have unique, often life-saving medicines, Novartis is committed to providing access for those most in need through access-to-medicines programs. These programs provide assistance to patients experiencing financial hardship or to those in the developing world who would not otherwise be able to receive treatment.

DELIVERING SUPERIOR OUTCOMES

The increasing focus by payors on treatment outcomes has drawn attention to the vexing issue of compliance: understanding why up to half of patients being treated for chronic conditions fail to take their medicines as directed. In cases where we can t prevent the disease, we need new approaches to drive compliance and reduce the significant number of patients who stop taking their medicines, says Joseph Jimenez, Head of the Pharmaceuticals Division and member of the Executive Committee of Novartis.

Reclast/Aclasta, a once-yearly medicine for osteoporosis developed by Novartis, improves compliance for all patients treated. By contrast, in some studies, less than a third of women prescribed daily tablets in the same class of medicines, known as bisphosphonates, still were taking their medication after 12 months. Novartis is so confident that better compliance will translate into superior patient outcomes that it has offered a money-back guarantee to health authorities in Germany. Novartis will refund the costs of *Reclast/Aclasta* to health insurers if a patient experiences an osteoporotic fracture within a year of an *Reclast/Aclasta* infusion.

Under a new risk-sharing model, Novartis is supporting an initiative by

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Britain s NHS to achieve superior outcomes in treatment of hypertension. The NHS has introduced a Quality-Outcomes Framework, offering financial incentives to physicians to achieve preset targets in treatment of patients. These targets sometimes are based on processes for example, the percentage of diabetic patients receiving annual eye and foot examinations. Incentives also reward a physician if a certain proportion of patients under treatment reach a preset blood pressure target.

Through the *Diovan* Guaranteed Target Initiative, Novartis is sharing the risk of achieving this blood pressure outcome with physicians. If patients treated by a physician fail to reach the blood pressure target with a treatment based on *Diovan*, Novartis will refund a portion of the medication cost.

EARLY ENGAGEMENT WITH PAYORS

In another step to improve patient access, Novartis is pioneering early engagement with health-technology assessment (HTA) agencies.

In 2008, when NICE indicated an interest in dialogue with companies prior to the formal assessment process for a new drug, Novartis followed up the overture and established a pilot project with the agency. The question we asked was, what kind of information and data are needed to enable NICE to come to an opinion about reimbursement of a new medicine as soon as possible? says Martin Backhouse, Ph.D., Head of Health Technology Assessment at Novartis. By having these discussions at a stage when we are still planning the pivotal phase of clinical testing, we would have flexibility to modify trial design to provide the data that the agency needs.

Early interaction with NICE and other health-technology assessment agencies is modeled on regular discussions pharmaceutical companies traditionally have had with regulatory agencies about design of clinical trials. Novartis developed a clear process for supplying the relevant information to the HTA agencies that, in turn, can provide advice about which aspects of the evidence are required to support a fast review of submissions when the product is approved by regulators.

These are not early price negotiations, Dr. Backhouse adds. Our discussions might involve showing that a new treatment from Novartis is better than existing therapies; which patient population would be most suitable for treatment; the duration of treatment that should be used in clinical trials; and whether we need to conduct a direct head-to-head comparison against the current standard of care.

Media coverage of the pilot project with NICE in 2008 prompted overtures to Novartis from other agencies interested in similar discussions. So far we have worked with seven pricing and reimbursement agencies in five countries, Dr. Grueger says. More such interactions are planned.

CLINICAL STUDIES IN EMERGING COUNTRIES

As it expands in many emerging markets, Novartis plans to increase the number of clinical trials conducted in those countries to forge even closer links with patients and physicians and enhance access to new Novartis medicines.

Local trials contribute to enhanced access for patients because authorities sometimes require studies in local populations as a precondition for regulatory approval. We conduct clinical studies only in countries where we intend to bring the product under investigation to the market if it proves to be effective and safe, says Detlef Niese, M.D., Head External Affairs, Global Development at the Novartis Pharmaceuticals Division. That s an important element of patient access.

Clinical trials may also contribute to further development of local healthcare

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systems. By participating in international clinical trials, local physicians become familiar with different kinds of healthcare practices, diagnostic procedures and the fundamentals of good clinical practice. In that way, expanding clinical research in emerging countries can help develop local healthcare systems over time, Dr. Niese adds.

But expanding clinical trials in emerging countries also can pose vexing ethical questions for Novartis. Poor education, poverty and lack of healthcare access can make it difficult for patients to provide the free, informed consent to trial participation that is a fundamental ethical principle of clinical research. There is a likelihood, for example, that if people have no health insurance, they see participation in a clinical trial as an opportunity to obtain treatment otherwise not available, rather than as a way to answer important scientific or medical questions, Dr. Niese says. In that case, their consent might not be a valid, free decision.

For Novartis, he adds, The key issue is that we have policies and practices in place in these countries to ensure that our clinical trials enroll only people who are able to give valid informed consent.

Novartis designs and conducts all clinical trials worldwide in accordance with the principles embodied in the Declaration of Helsinki, an internationally recognized statement of ethical guidelines for participants in medical research. All clinical trials at Novartis are conducted in agreement with other applicable national and international laws and guidelines. Novartis also pledges to respect the independence of researchers and their freedom to participate in and approve all aspects of a clinical trial, including the results.

Novartis ensures that its own medical and technical staff around the world, as well as external partners such as clinical investigators or medical sites, are capable of conducting clinical trials according to in-house and international standards. Local Development organizations at the country level also work closely with global Development functions at Novartis headquarters to provide support for clinical trial logistics, compliance with regulatory requirements and quality assurance.

Dr. Niese acknowledges that the cost of conducting clinical trials in emerging countries usually is significantly lower than in the United States or Western Europe. Novartis, however, takes great care that the same ethical principles are applied worldwide. It s important that a trial not be conducted in an emerging country because regulations are less developed or research participants less protected, he adds. Indeed, clinical studies by Novartis in emerging countries usually allay such ethical concerns by being part of broader international clinical programs, and by ensuring that all patients in all countries are treated the same.

Moreover, Novartis is taking additional steps to ensure that key decisions on clinical trials are taken in consultation with local communities. In 2007, Novartis established an Ethics Council in China, in collaboration with the Health Science Center at Peking University. The council is a group of independent ethicists, lawyers and specialists in clinical research who review Novartis policies, practices and protocols from a local perspective.

It s a way to avoid making decisions about clinical studies in an ethical or cultural vacuum, Dr. Niese says. The more transparent we are, the better it will be. And if this project is successful, it may serve as a model for other countries.

NOVARTIS VACCINES INSTITUTE FOR GLOBAL HEALTH

Vaccines against infectious diseases save the lives of an estimated 2 million children every year, but an additional 2.5 million still die from diseases preventable by vaccines. According to the World Health Organization, vaccination is one of the most cost-effective health investments, and there is an urgent need for vaccines against many neglected diseases that take a heavy toll in the developing world.

In 2007, Novartis opened the Novartis Vaccines Institute for Global Health (NVGH), a new research institute with a nonprofit mission of focusing exclusively on vaccines against diseases of the developing world. The institute, based in Siena, Italy, is the first of its kind to be established by a major vaccine manufacturer.

It is the goal of NVGH to discover vaccines specifically tailored for the needs of developing countries and to license development to third parties. All vaccines discovered by the institute that receive regulator approval will be introduced first in developing countries, and provided at an affordable and accessible price to populations of the developing world.

The mission of NVGH mirrors the Singapore-based Novartis Institute for Tropical Diseases (NITD), established in 2003. Both institutes focus on research and early stages of development, to the point of proof-of-concept in humans. And medicines discovered at NITD will be made available to countries in which the diseases are endemic at no profit to Novartis.

Research activities at NVGH center around conjugate vaccines for enteric, or intestinal, diseases. Initial priorities for NVGH are major causes of infection and disease in children, including Salmonella enterica serovar Typhi, Salmonella paratyphi A and nontyphoidal salmonellae (NTS). In Africa, resistant NTS is a major killer of children younger than 5 years old, second only to pneumococcal disease.

NVGH will have dedicated management, scientists and resources and access to expertise and innovative technology platforms at the Novartis Vaccines and Diagnostics Division s global research center, also in Siena.

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NOVARTIS ACCESS-TO-MEDICINE PROJECTS 2008

Project	Objective	Target region	Value (USD millions)	Patients
Malaria/WHO(1)	Provide *Coartem* at cost for public sector use	Africa, Asia, Latin America	263	70 000 000
Leprosy/WHO(2)	Eliminate leprosy by providing free medications to all patients worldwide with WHO, through 2010	Global	7	340 000
Tuberculosis(2)	Donation of fixed-dose combinations	Tanzania, Sri Lanka	1	44 000
Fasciolasis(3)	Providing free of charge *Egaten* to treat patients that are infected with Fascioliasis	Peru, Yemen	0.3	212 000
Novartis Foundation for Sustainable Development (N FSD)(4)	Improve health and quality of life of poor people in developing countries through think tank, policy and project work	Developing countries	9	3 002 000
Novartis Institute for Tropical Diseases (NITD)(4)	Discover novel treatments and prevention methods for major tropical diseases; NITD discoveries to be available in poor endemic countries without profit	Developing countries	14	
Novartis Vaccines Institute for Global Health (NVGH)(4)	To develop effective and affordable vaccines for neglected infec−tious diseases of developing countries	Developing countries	4	
US patient assistance program (PAP)(2) *(excl. Gleevec)*	Assistance to patients experiencing financial hardship, without third-party insurance coverage for their medicines	United States	107	81 000
Gleevec US PAP(2)	Within capability of Novartis, continue to ensure access for patients in the US who cannot afford the drug	United States	77	4 000
Glivec Global PAP(2),(5)	Within capability of Novartis, continue to ensure access for patients outside the US who cannot afford the drug	Global (excluding US)	751	23 000
Together Rx Access	Discount program for the uninsured	United States	0.4	7 000
Emergency relief & other product donations	Support to humanitarian organizations	Global	25	
Total			**1 259**	**73.7 million**

(1) During 2008, 70 million *Coartem* treatments reached patients based on a preliminary analysis of local distribution; Of these, 30.2 million treatments came from shipments completed in 2007, and 39.8 million from the total shipment of 73.8 million treatments completed in 2008. The value of the *Coartem* program in 2008 was calculated using the number of treatments shipped in 2008 and the ex-factory price of *Coartem* to private-sector purchasers in malaria-endemic developing countries, minus payments to Novartis to cover costs under terms of the public-private partnership with WHO. These payments were received through WHO, UNICEF and other procurement agencies, acting on behalf of governments and other public-sector institutions in developing countries eligible to receive *Coartem* at the not-for-profit price.

(2) Ex-factory price to private market

(3) At manufacturing costs

(4) Novartis operating costs

(5) Value includes donations under shared contribution and co-pay models, whereas patients in shared contribution and co-pay models are not included in the number of patients reached

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COARTEM

Malaria is a devastating disease that affects between 300 million and 500 million people and causes a million deaths annually. Its toll is heaviest among young children and adolescents in Africa. In addition to being Africa s worst childhood killer, malaria also causes the deaths of up to 10 000 mothers every year.

Under a unique public-private collaboration with international organizations, Novartis provides *Coartem* to the public sector without profit. To date, Novartis has provided 216 million treatments of *Coartem*, helping to save the lives of an estimated 550 000 people suffering from malaria.

In April 2008, Novartis announced a 20% average reduction in the price of *Coartem* tablets, our state-of-the-art artemisinin-based combination treatment (ACT) for malaria. To ensure a dependable supply and meet rising demand for *Coartem*, Novartis has invested heavily to expand production in China and the United States. Increased efficiency at these production sites made the price reduction possible.

The price reduction to USD 0.37 for children s doses will increase access to *Coartem* for millions of malaria patients, especially children in low-income regions of Africa. *Coartem* is well-tolerated and highly effective, providing cure rates of up to 95% even in areas of multi-drug resistance. Combining two or more malaria drugs has the potential to prevent or delay development of resistance to the disease.

Focusing on children in Africa, the group most vulnerable to malaria, Novartis has developed a more convenient formulation of *Coartem* as a powder that can be dissolved in milk, water or other liquids. The new dispersible formulation promises to make dosing more reliable than the current practice of crushing tablets for use by children. And a cherry flavor developed for the dispersible formulation helps mask the bitter taste *Coartem* shares with most other ACTs.

In December 2008, Swiss health authorities approved the new pediatric formulation of *Coartem*. The dispersible formulation is a joint development by Novartis and Medicines for Malaria Venture, a nonprofit foundation dedicated to the development of affordable new antimalarials.

GLEEVEC/GLIVEC PATIENT ASSISTANCE PROGRAMS

Ensuring access to treatment is particularly important in life-threatening diseases such as cancer, and Novartis is deeply committed to helping patients gain long-term access to our life-extending cancer therapies. We actively facilitate and support collaboration among the public and private sectors, to help patients get the medicines they need.

Providing access to cancer treatments is complex, demanding collaboration and compromise among industry, government, insurers and other payors as well as physicians and patient groups. Our experience shows that the most sustainable and efficient access is achieved through existing

local healthcare systems. Our access initiatives are customized to address local needs and leverage local infrastructure.

Globally, almost 200 000 patients have been treated with *Gleevec/Glivec* since its initial approval in 2001. In 2002, Novartis introduced the *Gleevec/Glivec* International Patient Assistance Program (GIPAP) that provides *Gleevec/Glivec* by full donation to properly diagnosed patients who have chronic myeloid leukemia or gastrointestinal stromal tumors, live in countries without government or private reimbursement or are unable to pay for the medication. To date, GIPAP has helped almost 35 000 patients obtain treatment without cost.

As the economic, healthcare and social dynamics of emerging countries evolve, Novartis Oncology continually explores new ways to maximize affordable and sustainable access to *Gleevec/Glivec* for a broader group of patients by pursuing innovative public-private partnerships. Today, the Global Patient Access Programs for *Gleevec/ Glivec* comprise a range of flexible models through which Novartis partners with national and local governments, charitable organizations or other payors.

Novartis also seeks ways to work with nongovernmental organizations, foundations, physicians and other health providers to achieve a common goal: the best cancer care possible for the greatest number of patients.

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COMMITMENT TO PATIENTS: TARGETS AND RESULTS FOR 2008 AND TARGETS FOR 2009

Stakeholder Engagement

Targets 2008	Results 2008	Targets 2009
Embed concept of consulting with key patient groups in the development and marketing cycles of major brands and therapy areas. Increase involvement of Novartis in civil-society debate on access to medicines.	Collaboration with major international patient groups was established for all therapy areas. More patient advocates are included on advisory boards, used to help develop clinical program and launch strategies. Increasingly, patient-group leaders and representatives are invited to Novartis management meetings, providing deeper insights into patient needs. Participated in the SustainAbility Pharmafutures project on improved health outcomes in emerging markets. Actively engaged in the Intergovernmental Working Group debate on access to medicines.	Continue to embed patient advocates as partners in advising on drug development and launch plans. Further collaborate on projects with major international patient groups to help raise awareness on burden of disease and patient needs. Continue involvement of Novartis in civil-society debate on critical topics with relevant stakeholders.

Access to Medicines

Targets 2008	Results 2008	Targets 2009
Launch pediatric dispersible formulation of *Coartem*. Facilitate data collection and publication of studies showing health impact of *Coartem* use.	In December, Swiss health authorities approved the new pediatric formulation of *Coartem*. The launch will occur during 2009. Published and presented data on the health impact of *Coartem* at international symposia. Continued and increased supply of *Coartem* without interruption. Reduced production cost of *Coartem* to further reduce price significantly.	Launch pediatric dispersible formulation of *Coartem*. Pursue efficient production of *Coartem* with uninterrupted supply. Collect data on the experience of using the new pediatric dispersible formulation of *Coartem* in endemic countries. Expand the Indian pilot of Arogya Parivar business model, that provides health education and makes quality medicines accessible and affordable to underserved rural regions.

Novartis Institute for Tropical Diseases

Targets 2008	Results 2008	Targets 2009
Fully consolidate Institute s new ventures Eijkman Institute; Hasanuddin University Clinical Research Institute (NEHCRI); and malaria research while continuing the buildup of the pipeline in dengue fever, tuberculosis and malaria. Maintain vigorous teaching and training activity, as well as high international scientific presence in tropical diseases research and development.	NEHCRI fully functional. First compound for malaria entered preclinical development and compound for dengue fever progressed further in preclinical development. Second class of students from Asia, Africa and Europe successfully completed MSc collaborative program with National University of Singapore, Swiss Tropical Institute and University of Basel. NITD hosted four international conferences and workshops.	Translate preclinical study findings in dengue fever, tuberculosis and malaria into strategic clinical development programs. Continue expansion of pipeline in all three disease areas. Maintain dynamic teaching and training activities, as well as significant scientific international presence in tropical diseases research and development.

Novartis Vaccines Institute for Global Health (New Target)

Targets 2008	Results 2008	Targets 2009
	Institute inaugurated in February 2008 with commissioning of first laboratories. Started first projects for vaccines in neglected diseases of the developing world (salmonella) by staffing the technical development and clinical trial functions.	First vaccine (a conjugate for typhoid fever) enters pilot-scale GMP (good manufacturing practices) production. Prepare start of clinical trials in 2010. Develop process for pilot-scale GMP production in 2010 for vaccines for paratyphoid in Asia and non-typhoid salmonella in Africa.

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COMMITMENT TO PEOPLE AND COMMUNITIES

The next generation of Novartis leaders will be more diverse and more global. Expansion in emerging markets will put a premium on recruitment of the relatively limited number of local executives with the international experience and skills required to work successfully in a global company such as Novartis. To attract and retain talent, employee engagement is a top priority, and the diverse portfolio of healthcare businesses at Novartis offers new recruits opportunities for rapid career development.

Future economic growth will demand more talented associates and leaders, yet the market for future talent will become increasingly competitive. Shifting demographic trends will result in fewer students, fewer graduates and fewer people entering the workforce in the Western world during the next 10 years. Supply of talent for key functional and leadership positions is waning, and a talent gap is clearly visible for some professions and geographies engineers in Germany, for example. Recruitment is increasingly regional or global in specialized fields such as clinical development, biosciences, chemistry and information technology.

Emerging markets are expected to be a driving force in global growth, but in countries such as Russia and China there is a limited pool of executives with the international experience and the language and other skills needed to work successfully in a global company like Novartis. Moreover, younger generations around the world have changing expectations about careers, engagement and the integration of work in their overall lifestyles. Geographic mobility is expected to decrease and talented workers in emerging countries anticipate ample career opportunities closer to home than in the past.

The next generation of Novartis leaders will be more diverse and global, says Juergen Brokatzky-Geiger, Ph.D., Head of Human Resources and member of the Executive Committee of Novartis.

To attract and retain scarce talent, employee engagement will be atop priority. International surveys indicate that corporate citizenship programs as well as diversity and inclusion strategies are key drivers of employee engagement, along with opportunities to improve skills and capabilities, areas in which Novartis scores above benchmarks and norms.

The well-established global Organization and Talent Review (OTR) process enables Novartis to identify, assess and develop associates with high potential. In 2008, 76% of the open positions at the Corporate Executive Group (CEG) level the 350 most senior executives at Novartis were filled with internal candidates, underscoring our focus on internal development of talent.

DIVERSITY AND INCLUSION

By many measures, Novartis already is a highly diverse organization. The CEG includes 27 nationalities. The proportion of female CEG members employed by Novartis Group companies worldwide has climbed to nearly 20% from 10% in 2005. Two of the 11 members of the Novartis Board of Directors are women. There has been notable improvement at Sandoz, our generic pharmaceuticals Division, where women now comprise almost 21% of CEG members employed by Group companies in the Sandoz Division, up from zero only three years ago. The Novartis Institutes for BioMedical Research, our

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pharmaceutical research unit, also have seen a rapid transformation, with women now comprising 18% of the CEG population employed by Group companies of NIBR, compared to 8% in 2005.

The Diversity and Inclusion Advisory Council (DIAC), created in 2006, comprises a group of external experts who advise Novartis on development and implementation of diversity and inclusion strategies and practices. In addition to academics, the DIAC includes businesspeople with direct experience of establishing diversity programs in global businesses. DIAC members also hold open meetings with associates and meet semiannually with Novartis business and diversity leaders to both support and objectively challenge company activities and progress.

Divisions and business units have developed strategies and action plans for diversity and inclusion, based on local situations and business cases. Targets for diversity and inclusion have been integrated into objectives of senior Novartis managers around the world.

Diversity and inclusion initiatives aim to make Novartis better reflect the heterogeneity of customers and stakeholders around the world. A diverse organization is more likely to be a creative environment because the ability to learn new things often comes from differences in views, backgrounds and beliefs, says Daniel Vasella, M.D., Chairman and Chief Executive Office of Novartis. We have to do an even better job of bringing in people from geographies where we have a large and growing presence but under-representation in management and leadership. We have a responsibility to ensure not only that they are identified, but also supported, so they can grow within the organization.

BRAZIL: AGILITY AND ENERGY

At the beginning of the decade, Brazil adopted legislation requiring companies to step up recruitment of people with disabilities. At all companies in Brazil with more than 1 000 employees, disabled people should comprise a minimum of 5% of the workforce. Failure to comply with the new law can result in penalties, including heavy fines and exclusion from government tenders for healthcare products.

The Novartis organization in Brazil had only two disabled employees prior to passage of the law, but an aggressive recruitment campaign added more than 80 disabled people to the payroll, close to the 5% target that must be reached by December 2009. The majority has physical disabilities, including impaired hearing and vision, but the Brazilian unit also has hired two employees with learning disabilities.

The new recruits have been deployed across the Novartis organization in Brazil in many customer-facing positions as well as in production and back-office jobs. The disabled employees we brought into the company are contributing members of the team, says Paula Traldi, Head of Human Resources at the Brazilian unit of Novartis. Interacting with disabled people daily provides insights about health and the kind of pressures faced by caregivers that can be applied to many other diseases. It has brought us closer to our customers and will give us a competitive advantage.

More than 20% of the disabled employees are sales representatives, and many have forged unusually close relationships with the healthcare professionals on whom they call. One physician in Sao Paulo wrote to Novartis extolling the agility and energy of sales representative Claudio Roberto Figueiredo. Because of his professional attitude, Claudio and Novartis stand out from other companies, the doctor added. I had never noticed that Claudio was disabled until one day he apologized because his two prosthetic ankles were making a bit of noise.

Successfully integrating people with disabilities into teams across the company has expanded the experience of associates, and enriched the spirit and culture of Novartis in Brazil, says Alexander Triebnigg, Head of both the Country Organization and Country Pharmaceuticals Organization in

FLUCTUATIONS 2008(1)

Associates as of January 1,2008	**98 200**	**100%**
Separations	-4 644	-5%
Retirements	-919	-1%
Resignations	-9 262	-9%
External hirings	13 342	14%
Associates as of December 31, 2008	**96 717**	**99%**

(1) Fuctuation percentage based on beginning of year balance

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Brazil. And it sends a positive signal about diversity and inclusion to the public, government agencies and customers.

EMERGING MARKETS

Recruitment and retention in China and Russia are fiercely competitive due to rapid economic growth and the imbalance in supply and demand of talent.

One important pillar of engagement for Novartis in China is the Beijing International MBA program, a mini-MBA curriculum at Peking University tailor-made for Novartis middle management. More than 250 associates have either graduated or are currently participating in the program.

In 2008, a similar program was launched to teach future Novartis leaders in Russia. The Novartis Business Academy is a program managed by Sweden s Stockholm School of Economics comprising 10 four-day modules in 12 months to develop midlevel managers in areas ranging from leadership and strategy to marketing, finance and project management. The current class at the Academy includes 40 employees based in Russia, representing all Novartis divisions.

Foreign assignments are another effective retention tool. Since 2006, 20 managers from China have taken part in the Trailblazer program which offers one-year rotations in the United States. A select group of high-potential managers in emerging growth markets was tapped for the Accelerated Development Program (ADP), designed to groom them for challenging new roles throughout the global organization. Executives selected for the ADP program are considered likely candidates for promotion, which could involve transfers to posts in another Novartis Group company such as divisional country head in a top-10 market within the coming five years.

The diverse portfolio of healthcare businesses at Novartis offers additional opportunities for career development. Cross-divisional staffing centers are being established in China and Russia to foster career mobility among divisions and across countries, providing broader experience for promising executives. Traditionally, cross-divisional talent exchange has been limited due to the lack of formal mechanisms to leverage talent-review programs across organizational boundaries.

A SAFER WORKPLACE

Novartis fosters a culture of safe behavior and on-site health promotion. Ongoing training programs for associates aim to bring Novartis closer to its goal of zero accidents. Diverse health-promotion activities are offered at many sites and Occupational Safety and Occupational Medicine teams work together to influence safe behavior and ensure health in the workplace.

Developing a strong safety mindset among associates also is a priority. In 2008, the lost-time injury and illness rate (LTIR) for continuing operations declined to 0.34 per 200 000 hours worked from 0.42 the previous year. As recently as 1997, the LTIR was 1.6 per 200 000 hours worked.

The improvement in workplace safety was achieved through preventative processes such as systematic use of workplace health-risk assessments. An increasing number of Novartis sites had no incidents with lost time. However, we deeply regret the death of one Novartis associate in a traffic-related accident during 2008. We extend our condolence to the family.

As the number of accidents leading to lost time decreases, our focus will shift to reducing accidents leading to injuries in general. This number, called the total recordable case rate (TRCR), was reported in 2007 for the first time. In 2009, a target has been set for a 10% reduction from 2008 levels. A further reduction of LTIR in 2009 is envisioned from an actual rate of 0.34 to 0.31.

ASSOCIATES BY REGION AND DIVISION AS OF DECEMBER 31, 2008(1)

	United States	Canada and Latin America	Europe	Asia/Africa/ Australasia	Total
Pharmaceuticals	13 546	4 391	24 044	11 651	53 632
Vaccines and Diagnostics	1 018	8	3 578	170	4 774
Sandoz	1 161	2 594	15 021	4 370	23 146
Consumer Health	3 812	1 447	4 651	3 104	13 014
Corporate	792	47	1 095	217	2 151
Total	**20 329**	**8 487**	**48 389**	**19 512**	**96 717**

(1) Full-time equivalent positions

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COMMITMENT TO PEOPLE AND COMMUNITIES: TARGETS AND RESULTS FOR 2008 AND TARGETS FOR 2009

Living Wages

Targets 2008	Results 2008	Targets 2009
Continue to use established process for periodic updates of living-wage levels and adjustment of salaries of associates who are below those levels.	The wage-level review identified three cases globally that required adjustment to the living-wage level.	Continue using established processes to update living-wage levels annually and adjust salaries of associates who are below those levels.

Global Employee Survey

Targets 2008	Results 2008	Targets 2009
Plan an aligned approach for the Novartis Global Leadership survey and annual employee climate survey to allow synchronized implementation in 2009.	A global employee survey instrument was designed with focus on engagement across all levels.	Administer the Novartis Global Employee Survey in March 2009. Communicate findings to associates and implement follow-up actions.

Diversity and Inclusion

Targets 2008	Results 2008	Targets 2009
Continue to use the external Diversity and Inclusion Advisory Council (DIAC) as implementation aid. Continue divisional and functional implementation, according to business needs.	The DIAC is an established body supporting and challenging Novartis efforts in diversity and inclusion, particularly in the areas of talent development and marketing strategies. Divisions have created diversity and inclusion strategies and action plans.	Leverage diversity and inclusion to enhance marketing effectiveness, improve integration of diversity and inclusion in talent development and improve training programs on diversity and inclusion. Further implement employee resource groups, diversity-specific mentoring programs and awareness training programs. Establish training for fair and objective recruitment.

Lost-Time Injury and Illness Rate (LTIR)

Targets 2008	Results 2008	Targets 2009
Reduce LTIR to 0.39.	0.34.	Reduce LTIR to 0.31.

Total Recordable Case Rate (TRCR)

Targets 2008	Results 2008	Targets 2009
Baseline measurement.	1.08.	10% improvement by end 2009, based on 2008 level.

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COMMITMENT TO THE ENVIRONMENT

Measures implemented by Novartis Group companies to reduce greenhouse gas emissions have proven their effectiveness. A proactive policy for capital investment in energy conservation is an example of strong support from senior management for energy efficiency, and carbon-dioxide-mitigation programs.

Activities related to the environment at Novartis during 2008 focused on improving energy efficiency and reducing carbon dioxide (CO_2) emissions.

Our long-term commitment to the environment was recognized again when Novartis was named super sector leader for healthcare in the 2008 update of the Dow Jones Sustainability World Index (DJSI World), a global index tracking the performance of sustainability-driven companies worldwide. The annual review of the DJSI is based on economic, social and environmental performance. Among environmental indicators, Novartis received 100% scores from DJSI for both reporting and policy/management system.

EXEMPLARY SUSTAINABILITY

With its energy-saving programs and a stellar safety record, our site in Kundl, Austria, is one of the best examples of how principles of Corporate Citizenship are integrated into day-to-day operations.

Kundl began production of penicillin in 1946 in premises previously used for brewing beer. More than six decades later, it is the only remaining antibiotic developer and producer in Western Europe or the United States.

Sandoz, the generic pharmaceuticals Division of Novartis, has managed to buck the exodus of antibiotic makers to low-cost countries in Asia through consistent productivity gains, including continuous refinement of the bacterial strains in which antibiotics are grown.

Energy use is a major concern at the Kundl site because the key production process fermentation is an energy-intensive technology. Sandoz accounts for more than 40% of annual Groupwide energy consumption while Kundl alone is responsible for about 30% of the division s energy outlays.

Large amounts of electricity are required to ensure air supply to nutrient broths and to drive rotors stirring broths in giant fermenters with capacity of up to 250 cubic meters. The energy we put into production is a cost, and today it is increasingly seen as being detrimental to the environment and a potential liability for our brand, says Ernst Meijnders, Head of both the Kundl site and the Anti-Infectives Business Unit of Sandoz.

In response to such challenges, energy efficiency initiatives within Kundl s fermentation unit have been acknowledged with Novartis Energy Excellence Awards in three of the past five years. These projects have improved economics of production of penicillin V and cephalosporin, both large-scale fermentation processes. Savings in electricity consumption represented 6% of total energy usage by the Kundl site in 2006 and 4% in 2008. Upfront investments of USD 6.7 million have delivered annual savings of USD 8.3 million.

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In 2006, Kundl was acknowledged for a behavior-based energy-efficiency initiative implemented at a manufacturing unit for pharmaceutical products.

Encompassing more than 30 individual projects, this initiative helps to improve energy efficiency through changes in associates behavior rather than technological breakthroughs. The payoff has been annual savings totaling USD 500 000 in return for an initial investment of USD 250 000. Importantly, the behavior-based program was easy to expand across the Kundl site and also can be replicated at other Novartis production sites around the world.

Changing behavior also was the objective of a parallel program focusing on safety. This behavior-based safety initiative has enabled Kundl to achieve significant improvement in its lost-time injury and illness rate (LTIR), the principal safety benchmark used at Novartis production facilities. The site halved its LTIR between 1994 and 1998 to 1.2 accidents per 200 000 hours from 2.5 accidents four years earlier. In 2008, Kundl s LTIR reached 0.28.

To improve quality, energy efficiency or safety, you obviously need the right technology and equipment as well as the right processes. And it s important to have the right performance rewards, Mr. Meijnders says. But it s also critical to foster the right mindset among your people.

Building that mindset starts with a staunch commitment from senior management. The behavior-based safety effort has raised awareness through training of 300 Kundl managers on a new safety policy. An annual agenda of more than 600 audits has been established to deter unsafe behavior.

Monthly meetings of Kundl s management safety committee are attended by representatives from line management, associates, and the site s works council.

Following an accident, the head of the department involved appears at the safety management meeting to describe what happened, give an update on the associate s condition, explain how the accident was handled, and reach agreement about potential remedial steps. A database describing accidents is accessible for all associates at the Kundl site; flyers communicating the site s safety record are distributed regularly to associates.

Moreover, Kundl associates are allowed time during working hours to meet, think creatively about safety and discuss improvements. When they come up with strong proposals, they receive resources to implement them. We try to put up challenging targets and give people opportunities to participate and contribute, Mr. Meijnders says. It s the way to secure buy-in which ultimately is responsible for the mindset change.

ENERGY EFFICIENCY

Novartis has ambitious energy and climate targets with a high priority on energy efficiency and reduced greenhouse gas (GHG) emissions. In 2005, Novartis voluntarily committed to the Kyoto Protocol the international agreement among countries that sets binding targets for reducing GHG emissions by an average of 5% against 1990 levels by 2012. Programs to improve energy efficiency and reduce GHG emissions are beginning to bear fruit. Scope 1 GHG emissions from Novartis sites declined to 404 kilotons in 2008 from 408 kilotons the previous year, despite buoyant growth of Group sales.

For an expanding company like Novartis at the forefront of science, it is a challenge to cut back on carbon emissions, especially because we operate in a low energy-intensive industry, says Keith Saveal, Head Corporate Health, Safety, and Environment and Business Continuity. But increasing energy efficiency is a way of life at Novartis. We want to be a leader in tackling global environmental problems. Moreover, in the face of the prospect

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of a long- term rise in energy costs, increased energy efficiency and a reduced carbon footprint simply make good business sense.

Measures implemented to date to reduce GHG emissions have proven their effectiveness. As part of the ongoing transformation of Novartis headquarters in Basel from an industrial site to a state-of-the-art center for research, development and management, the new buildings require, on average, only about a third of the energy used by older buildings.

A proactive policy for capital investments associated with energy conservation exemplifies strong support from Novartis senior management for the energy efficiency and carbon-dioxide-mitigation programs. Payback periods up to the lifetime of the asset are allowed for projects that save energy. In addition, a review of energy-usage implications by an energy expert is mandatory for all investments or asset acquisitions exceeding CHF 20 000. Increasingly, divisions and business units are appointing energy managers for their worldwide operations while energy-management tools and dedicated training programs are being applied systematically, together with continuous monitoring of targets and performance.

We approach energy savings and reduction of carbon emissions on two key fronts, Mr. Saveal says. First, we have found many simple ways to increase our energy efficiency which has risen by more than 25% since 2003. The second is by investing in innovative energy conservation and renewable energy projects. We still have a long way to go, but we are continuing to identify new ways to make progress towards our energy and climate targets.

To help achieve these ambitious targets, Novartis has introduced a global Data Management System to facilitate data collection in line with more stringent reporting standards. This system provides Group managers with information needed to take early action if deviations against targets occur. The data includes GHG emissions from on-site, fossil fuel combustion and vehicles (all Scope 1); emissions from generation of purchased energy (Scope 2); as well as health and safety information.

GHG EMISSIONS 2003 2008 VERSUS TARGET PATH TO 2012

(in kilotons CO_2)

TRANSFORMING STRATEGY INTO MEASURABLE ACTION

Novartis set a target of a 10% reduction in CO_2 emissions from approximately 23 000 motor vehicles it owns or leases worldwide, compared to the 2005 level. In the United States the target will be achieved by switching to vehicles with hybrid gasoline/electric engines or other fuel-efficient technology. In Europe, Novartis now requires the use of diesel vehicles with particulate filters. In Germany, for example, Novartis has implemented financial incentives for sales representatives who drive fuel-efficient vehicles.

By 2008, emissions had been reduced by 3% from the 2005 level despite an increase in the size of the vehicle fleet.

Meanwhile, Novartis completed a project to define energy standards for new buildings and equipment during 2008. The goal is to ensure efficient, cost-effective and climate-conscious use of energy by applying both the best available technology and the concept of total cost of ownership. The new energy standards apply to building design, building structure and envelope, utilities, machinery, vehicles, lighting systems as well as heating, ventilation and air conditioning (HVAC). HVAC is one of the major sources of energy consumption at Novartis.

Combined heat and power plants (CHP) have become an important option as Novartis strives toward more efficient energy use. Overall efficiency of a CHP installation is about double that of a conventional plant. A CHP plant has recently been installed in Singapore and a second plant is planned for Germany.

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NOVARTIS HEALTH, SAFETY AND ENVIRONMENT (HSE) DATA 2008

	Novartis Group(1)		Pharmaceuticals (Excluding Research)		Novartis Research(2)		Vaccines and Diagnostics		Sandoz		Consumer Health	
	2008	**2007**	**2008**	**2007**	**2008**	**2007**	**2008**	**2007**	**2008**	**2007**	**2008**	**2007**
Employees												
HSE personnel (number of associates working at least 50% for HSE)	**491**	501	**216**	217	**26**	23	**37**	39	**147**	157	**65**	65
Health/Safety												
Lost-time injury and illness rate (LTIR) [per 200 000 hours worked]	**0.34**	0.42	**0.37**	0.45	**0.23**	0.13	**0.51**	0.74	**0.41**	0.53	**0.14**	0.23
Total Recordable Case Rate (TRCR) [per 200 000 hours worked]	**1.08**	1.41	**1.19**	1.68	**1.35**	0.68	**1.52**	2.29	**0.99**	1.28	**0.70**	1.02
Production												
Total production (1000t = metric tons)	**162**	171	**27**	27	**0**	0	**0.3**	0.3	**87**	94	**48**	49
Resources												
Water use (million m3)	**79.1**	83.6	**21.6**	21.8	**1.3**	1.1	**1.1**	1.1	**52.5**	57.0	**2.5**	2.6
Energy use (million GJ)	**16.9**	16.7	**5.7**	5.6	**1.0**	1.0	**1.2**	1.2	**7.5**	7.4	**1.5**	1.5
Emissions into water												