RESEARCH & DEVELOPMENT

Pfizer brings unparalleled breadth of scientific capabilities to bear on urgent, unmet medical needs. We believe our leadership in drug design, biotherapeutics and vaccines, small molecules and discovery and development sciences—together with our extensive network of external collaborations—will help open a new era of biomedical research. We are driving a bold R&D strategy to deliver the next generation of medicines and vaccines that will matter most to the people we serve, year over year.

Like all of our peers, Pfizer faces challenges that will shape the future of R&D and the future of the industry. We are responding with a vigorous strategy to strengthen our innovative core, focusing on the delivery of our portfolio, the development of important new capabilities, and the anticipation and creation of the R&D ecosystem of the future, which will seek to deepen innovation networks connecting industry, academia and the public sector.

To strengthen the delivery of our portfolio, we are moving forward with renewed methods to drive medically differentiated products that are commercially relevant. We also are deepening our knowledge of pathogenic mechanisms to drive greater therapeutic impact.

To develop important new capabilities, we are pushing the boundaries of how drugs will look in the future, and we are creating totally novel platforms for open and external innovation.

To lead the R&D ecosystem of the future, we are aiming to fully deliver on the promise of “Precision Medicines” across multiple therapeutic areas—as well as highly interactive and networked R&D.

Expanded internal and external capabilities, a strong focus on “Precision Medicines,” differentiated innovation and our commitment to thorough integration of science and business are designed to yield an important step change in productivity.

To accelerate these strategies, Pfizer has announced a series of measures to increase focus, expand externalization strategies and more strongly position the company for differentiated innovation.

2010 Highlights

1. An important example of “Precision Medicine” is crizotinib, which has advanced rapidly into Phase III trials. The novel compound targets the ALK gene mutation in certain advanced non-small cell lung cancer tumors. Pfizer expects to complete the U.S. submission of a New Drug Application for crizotinib in the first half of 2011.

2. Bosutinib is in Phase III trials in the U.S. for the treatment of chronic myelogenous leukemia.

3. Sutent has been approved in Europe for the treatment of pancreatic neuro-endocrine tumors.
We will concentrate on core research areas where we can deliver the greatest medical and commercial impact. These areas include neuroscience, cardiometabolic diseases, oncology, inflammation and immunology, and vaccines—all of which are augmented by the advantaged modalities delivered by our CovX and Rinat biotechnology units.

Specialized units will focus on pain and sensory disorders and on biosimilars. We will, furthermore, initiate external research programs in high-potential areas within Primary and Specialty Care. And in line with our disease-area strategy, our post-proof-of-concept portfolio will focus on high-priority disease areas and will include a mix of owned and partnered assets that together aims to improve our risk/return profile.

We are establishing industry-leading models for external collaboration that allow us to access the best science. We continue to establish strategic collaborations with industry and academia and look to expand the numbers and types of these collaborations. We joined with seven of New York City’s top research universities and hospitals to expand Pfizer’s Centers for Therapeutic Innovation (CTI) program. We have formed our first CTI partnership with the University of California, San Francisco and will co-locate Pfizer scientists there alongside their academic counterparts.

We will strengthen the fundamentals that drive differentiated innovation to deliver the medicines and vaccines that matter most. We are strengthening internal programs to drive disciplined decision-making and portfolio governance. Our R&D site network also will align more closely with key hubs for biomedical innovation, connecting our network more deeply with leading biomedical research institutions and providing us with more access to a deep talent base in science.

Pfizer scientists, along with our counterparts in many alliances and partnerships, are among the leaders in the global effort to incorporate innovative “Precision Medicine” strategies into all of our core and specialized research areas. “Precision Medicine” focuses on clusters of patients who share a genetic variation and thus would benefit from a specific therapeutic approach. For example, in oncology we are working on a variety of treatments—ranging from small molecule compounds to biologics to therapeutic vaccines—that target specific gene mutations in tumors.

Axitinib has demonstrated efficacy against metastatic renal cell carcinoma in Phase III trials.

Apixaban, an oral anticoagulant co-developed with Bristol-Myers Squibb, showed clear evidence of efficacy in a Phase III trial for atrial fibrillation. Meanwhile, it was submitted for approval in Europe for treating venous thromboembolism.

Taliglucerase alfa, a plant-based enzyme, has been submitted for approval in the U.S. and Europe for treating Gaucher’s disease, a rare, inherited condition. With permission from regulatory authorities, the treatment, being developed in partnership with Protalix, is already being made available to people suffering from this genetic disease.
Advancing the Pipeline

Pfizer’s pipeline of medicines in development is rich in Phase I and Phase II programs, backed by more proof of concept than ever before, and well-balanced between small molecules and large (protein-based) biologics and vaccines. We update our pipeline regularly—this chart reflects the pipeline update of February 28, 2011.

Collaborating on Research for Diseases of the Developing World

Many pharmaceutical companies, including Pfizer, are committed to biomedical research to improve health in both developed regions and in the developing world. Our efforts include research on medicines across multiple therapeutic areas, with academia, global health organizations, public-private partnerships and companies that share our commitment.

Pfizer supports research programs on public health issues associated with the developing world including research on tuberculosis, malaria and river blindness, and through our joint venture with GSK, ViiV Healthcare, on HIV/AIDS.

Working with the World Health Organization’s Special Programme for Research in Tropical Diseases, we provided broad access to Pfizer’s library of medicinal compounds to scientists from other organizations, and also trained scientists from developing countries to investigate new approaches to treating or preventing diseases. To expand screening efforts for tropical diseases such as African sleeping sickness and Chagas disease, Pfizer is collaborating with the Drugs for Neglected Diseases Initiative while pursuing a molecular approach for them with several UK universities.

For more information on ViiV Healthcare please visit http://www.viivhealthcare.com.

pNETS
Short for pancreatic neuro-endocrine tumors. Pfizer’s Sutent was approved late in 2010 by European regulators for treating these relatively rare tumors.
Tuberculosis (TB) continues to be a major global health problem, with an estimated 8.8 million new cases and 1.6 million deaths annually. Efforts to control and eradicate TB have been stymied by the spread of HIV/AIDS in TB-endemic regions, and by the global emergence of strains resistant to current TB drugs. To address this pressing medical need, we have been working with external partners to pursue new treatments.

We are currently evaluating a new compound, PNU-100480, which has successfully completed Phase 1 studies and will be starting first-in-patient studies this year. PNU-100480 is an oxazolidinone, a class of antimicrobials that inhibits bacterial protein synthesis. PNU-100480 is being developed to treat TB, including multidrug-resistant TB—a form of the disease that is emerging as a serious public health threat, and is especially lethal and difficult to treat.

Given the global nature of TB and the likelihood that a combination drug regimen will work most effectively against the highly complex disease organism, engagement with external partners is vital. Pfizer is actively participating in the Critical Path to TB Drug Regimens initiative, an innovative collaboration sponsored by the Bill & Melinda Gates Foundation that brings together public and private sectors to accelerate the development of new, safe and shorter duration TB drug regimens. We are also collaborating with various organizations to tackle two other challenges associated with TB: long duration of TB drug regimens, and negative interactions with HIV treatments.

TB is now the leading cause of death among patients with HIV/AIDS, accounting for roughly half a million deaths a year, according to the World Health Organization. Standard TB treatments such as rifampin can interact with the antiretroviral drugs used to treat HIV. Rifabutin, which is produced by Pfizer, does not interact with this class of medicines. As part of our commitment to increasing access to life-saving medicines, Pfizer and the Clinton Foundation HIV/AIDS Initiative are partnering to make rifabutin available to low-income populations in emerging markets.
Malaria afflicts up to 250 million people annually, killing close to 1 million people a year, mostly children in Africa.

We are providing the Medicines for Malaria Venture (MMV) access to Pfizer’s library of chemical entities to screen approximately 200,000 compounds that have the potential to be developed into new treatments against *P. falciparum*, the parasite that causes acute malaria, including multidrug-resistant strains. In collaboration with MMV and the London School of Hygiene & Tropical Medicine, we are in Phase III development of the combination of azithromycin and chloroquine as a potential intermittent preventive treatment of malaria for pregnant women in sub-Saharan Africa. Malaria in pregnancy is an area of high unmet medical need and is one of the most common preventable causes of maternal and infant mortality and morbidity in malaria endemic countries; approximately 30 million pregnant women are at risk for malaria in sub-Saharan Africa each year.
ViiV Healthcare, a company launched in 2009 by Pfizer and GlaxoSmithKline (GSK), focuses solely on research, development and commercialization of HIV treatments.

ViiV Healthcare integrates the pipeline and marketed HIV portfolios of both Pfizer and GSK, and is continuing the commitments of both companies to improve access to HIV medicines for everyone. Not-for-profit pricing for HIV medicines is being provided to those most in need—a total of 69 countries. To make antiretrovirals at lower cost for people in the Least Developed Countries, Low Income Countries and sub-Saharan Africa, ViiV has granted 11 voluntary licenses to Indian and African generic companies. ViiV Healthcare is also supporting research and development activities specifically to address HIV treatment challenges including treatments and formulations for children living with HIV, and managing a new fund to help prevent mother-to-child transmission.
**Conducting Clinical Trials to the Highest Standards**

Clinical trials are at the heart of biomedical progress, and we recognize that volunteers are unsung medical heroes of our day. We are working to enhance our clinical trial infrastructure to ensure that all of our trials are done to the highest standards and protect the rights and welfare of the trial participants who make our progress possible.

Wherever we conduct clinical trials, we do so in accord with the highest ethical, safety and scientific standards. Across a wide range of research units, therapeutic areas and diseases, approximately 2,000 Pfizer clinical and medical colleagues share responsibility for conducting hundreds of clinical trials involving thousands of investigators, research coordinators and study site personnel. Over 150,000 patients are involved in these trials.

Last year, we launched the Clinical Trial Excellence Initiative, a reengineering and quality improvement initiative to optimize the management of our trials to ensure quality and compliance across all of our clinical trials. This initiative, under the direction of a Pfizer senior vice president reporting to the company’s Chief Medical Officer, should be completed late in 2011. When it is, Pfizer will have additional state-of-the-art capabilities for clinical trial design, development and execution.

We have sponsored a number of initiatives with stakeholders and partners to help advance research integrity and ethics. For example, we convened a 50-organization summit on Global Clinical Trials that resulted in a white paper on opportunities for improving multiregional clinical trials, posted on Pfizer.com/development. We have been working with Harvard to establish a center on multiregional trials to implement some of these ideas and find others. We commissioned a clinical trial manual, “Reviewing Clinical Trials: A Guide for the Ethics Committee,” that was proposed and sponsored by Pfizer and authored by experts from the University of Hong Kong, the Association for Accreditation of Human Research Protection Programs (AAHRPP) and leading bioethicists from around the world. Finally, we were the first and only pharmaceutical company to pursue and obtain full AAHRPP accreditation of our Phase I clinical research units.

We are also committed to transparency in clinical trials. As of November 2010, we have registered more than 1,509 studies to clinicaltrials.gov and posted results of 1,090 studies on clinicalstudyresults.org.

**Global Standards**

We have run trials in over 60 countries, and increasingly in the developing world, which has unique challenges. To ensure patient safety and ethical conduct throughout the study, we follow global policies and standard operating procedures for our clinical trials wherever they are run. Our policies and processes require that informed consent, independent ethics review, post-study care and the use of placebos conform to established international ethical standards. To ensure informed consent, we have invested in programs such as “talking books” that illustrate the advantages and disadvantages of clinical trial enrollment in simple-to-understand words and illustrations.
We also engage in local capacity building. Capabilities of local investigators and research sites are carefully reviewed by a study team and can be included in the trial only if the investigators have sufficient knowledge, expertise and infrastructure to conduct a clinical trial in accordance with Good Clinical Practice. We provide training in Good Clinical Practice to all investigators and all sites. We have developed a certification program for our clinical research staff and contractors, with over 1,000 colleagues and contractors now having successfully completed this certification program.

To ensure ethical conduct, we have detailed monitoring plans for each trial, and review the data and human subject protection procedures at each site over the course of the trial. In 2010 Pfizer conducted over 50,000 monitoring visits at 13,000 sites around the world, as well as several hundred internal audits of these sites to assess adherence to good clinical practice and pharmacovigilance requirements. Regulators from the U.S., Europe, Japan and elsewhere also regularly audit our trials and the local trial sites in the U.S. and abroad, to ensure that the data is trustworthy. When we conduct trials that are blinded (that is, neither we nor the investigators know which patient is getting the study drug or a different drug), we utilize independent data monitoring committees (DMCs) if mortality or major morbidity is an endpoint or if there are other known safety concerns. The DMC provides an external assessment of interim data and advises us whether a trial may need to be suspended or terminated to protect patient safety. Last year, we had over 80 different data monitoring committees overseeing Pfizer trials around the world.

Improving the Odds to Deliver New Treatments, Cures and Vaccines

The overwhelming majority of compounds tested in the laboratory fail to move beyond the testing stage and only a relative handful move on to more advanced tests for efficacy and safety. Among those that do advance, many fail at the clinical trial stage. We are among the leaders in exploring and, where appropriate, using quantitative approaches to improve R&D productivity by picking likely “winners” earlier in the development process. In concert with regulators in the U.S. and elsewhere, Pfizer is advancing adaptive clinical trial approaches that may, over time, change the ways clinical trials are executed, and gain more information from the use of fewer human volunteers. We are even exploring programs that may harness massive computing power to create “virtual” clinical trials, giving indications early on how best to move ahead using human volunteers.

We are also working on innovative ways of conducting clinical trials with broadly distributed patient populations using remote monitoring and self-reporting. Initial efforts to test the concept focus on post-marketing (or Phase IV) clinical trials.
Bioethics

For close to two decades, we have been using animal and, more recently, adult stem cells in our laboratories to help screen new compounds and identify safer and more effective medicines. We acknowledge the sensitive ethical issues surrounding certain forms of stem cells and strongly oppose cloning of human embryos, but we believe that stem cell research, conducted in accordance with the highest ethical standards set by leading scientific authorities, is an important tool in the search for innovative new medicines.

With compelling evidence from this research, we have begun to explore accessing drug development technology from leading academic, biotechnology and pharmaceutical partners around the world, who also have experience with currently available human embryonic stem cell lines that meet the same high ethical standards that apply to our internal research. Pfizer’s Stem Cell Policy guides the company’s research activities and its exploration of new external partnerships.

Over two years ago, we launched a Regenerative Medicine Unit, whose mission is to build upon recent scientific progress in understanding the biology of all types of stem cells, and to leverage these opportunities to discover and develop a new generation of regenerative medicines for major medical needs. Through our work with strategic alliance partners, academic researchers and patient advocate groups, we seek to further develop these technologies and provide new therapies for patients around the world.

Animal Care and Use

Pfizer’s Animal Care and Use Policy reflects our absolute commitment that animals used in research are treated humanely. This means that any research involving animals is conducted only after appropriate ethical consideration and review. This review ensures that we provide a high level of care to experimental animals, and that there is no scientifically appropriate and validated alternative to the use of animals that is acceptable to regulators, where relevant. For as long as it remains necessary to use animals in biomedical research for the discovery, development and evaluation of new medicines, we commit to maintaining the highest standards in the humane treatment of these animals.

We are fully committed to the development and use of scientifically validated alternative testing methods that are acceptable to regulatory authorities and do not compromise patient safety or the effectiveness of our medicines. Pfizer continues to engage and lead cross-industry efforts aimed at developing and refining new in vitro testing and predictive informatics-based systems that hold promise for future reduction of animal usage. We work through pharmaceutical trade organizations and directly with regulators to increase the recognition and acceptance of alternative models where such alternatives can be used appropriately.