Chairman's review

Matthew Emmens—Chairman

A year of unprecedented change and enormous opportunity.

Those charged with leading Shire throughout 2009 entered the year fully cognizant of the challenges that lay ahead.

There were, to begin with, the pressures forged by an industry confronted by a nearly perfect storm—the worldwide recession; the implications of proposed healthcare reforms; and the increasing insistence, on the part of physicians, patients, and payers, that the benefits of medicines be wholly quantified. Value had become the watchword. The deliberate execution of well-made plans would separate those who merely stayed afloat from those who set new standards.

Such external pressures for our industry were compounded at Shire by the long-anticipated genericization of ADDERALL XR, the product that had fuelled Shire's rise as a leading specialty biopharmaceutical company. Certainly Shire had proactively planned for its post-ADDERALL XR era by bolstering its pipeline with a new generation of Attention Deficit Hyperactivity Disorder ('ADHD') drugs. Still, the stakes were high.

Staying on course in a weak economy with a portfolio that was no longer headlined by ADDERALL XR would require Shire to dig deep—to facilitate the kind of transformation one rarely sees in any industry, under any circumstances. Those of us who know this company—the breadth of its talent, the depth of its commitment—were not surprised by the results. In 2009 Shire did not just maintain its position as the world's leading branded ADHD company, it also advanced its portfolio of eight[1] growth-driving products (with robust intellectual property protection), extended its global presence to 28 countries, and, through its Human Genetic Therapies ('HGT') business, proved its capacity to answer to some very pressing patient needs. At the close of 2009, Shire remains on track to meet its aspirational targets of mid-teen digit revenue growth on average between 2009 and 2015.

Shire's product portfolio is young and growing. It features a number of 'best-in-class' medicines; medicines that make a discernible difference. VYVANSE, the once-daily ADHD medicine indicated for both children and adults, has surpassed the $1 billion mark in cumulative gross sales since its launch mid-2007. INTUNIV, launched this past November is a highly promising selective alpha-2A receptor agonist indicated for once-daily treatment of ADHD.

1 ELAPRASE, FIRAZYR, FOSRENOL, INTUNIV, LIALDA/MEZAVANT, REPLAGAL, VPRIV and VYVANSE.

2009 highlights

- VYVANSE surpassed the $1 billion mark in cumulative gross sales.
- ELAPRASE is treating patients in more than 40 countries around the world.
- LIALDA has 18% market share of the total US prescriptions for ulcerative colitis.
- FOSRENOL is now marketed in 38 countries.
- VPRIV was approved in the US 18 months ahead of schedule in February 2010 and advanced in registration in the EU at the end of 2009—product available on pre-approval basis.

LIALDA, already with 18% market share of the total US prescriptions for ulcerative colitis, is currently in global Phase 3 trials for diverticulitis, an indication that has twice the patient population potential of ulcerative colitis. We expect to complete this Phase 3 trial by the end of 2010 with a potential launch in early 2012. FOSRENOL, a phosphate-binding agent used in the control of hyperphosphataemia in chronic renal failure patients, was our first international product launch, and is now marketed in 38 countries. ELAPRASE, our Hunter syndrome product, is treating patients in more than 40 countries around the world. VPRIV (velaglucerase alfa), to help treat patients diagnosed with that most common of all lysosomal storage diseases, Gaucher disease, is now available on treatment protocol in the US and for compassionate use in the rest of the world; it has also been granted Priority Review by the US Food and Drug Administration ('FDA') and the product will be commercialized in the US at the end of February 2010, 18 months ahead of schedule.

The world in which we live and work is in endless flux. Going forward we expect to see physicians, patients, and payers benefiting from the new science of biomarkers and calling for—even demanding—far more specific agents to treat disease. We expect to see specialist physicians taking a more active role in the lives of their patients, and patients more proactively managing their own health. We expect to see an environment, in other words, that is ripe for the kind of company that Shire continues to become—'best-in-class', highly differentiated, forward thinking, truly innovative, and deeply concerned with the lives of those it serves.

For the past several years, as you will see in this report, Shire has positioned itself to take the right risks in a changing world. Today it finds itself in the midst of a growth cycle—fully supported by a flexible business model and staffed by a team that continues to demonstrate remarkable courage and dedication. Shire isn't done yet, and it does not wish to be. The transformation continues.

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Chairman