

WE AIM TO BUILD ON OUR POSITION AS A WORLD LEADER IN CANCER TREATMENT THROUGH CONTINUED GROWTH OF ARIMIDEX, FURTHER LAUNCHES AND LINE EXTENSIONS OF NEWER PRODUCTS SUCH AS FASLODEX, AND THE SUCCESSFUL INTRODUCTION OF NOVEL THERAPEUTIC APPROACHES CURRENTLY IN DEVELOPMENT, INCLUDING BOTH SMALL MOLECULE AND BIOLOGICAL DRUGS.

PRODUCTS

Arimidex continued its strong sales and prescription growth on the basis of the large-scale ATAC study, which first reported in 2001. Data presented at the San Antonio Breast Cancer Symposium in December 2007 showed that, in post-menopausal patients, *Arimidex* continues to be more effective than tamoxifen, with the difference increasing over time, even after a five-year treatment course. As initial adjuvant therapy, *Arimidex* is the only aromatase inhibitor shown to be significantly superior to tamoxifen at preventing all breast cancer events beyond the five-year treatment course. (Breast cancer events are defined as locoregional recurrence, distant recurrence or contra-lateral breast cancer).

In several large markets, *Arimidex* has already replaced tamoxifen as the preferred primary adjuvant treatment for post-menopausal women with hormone-receptor positive, invasive, early breast cancer. In 2007, *Arimidex* exceeded three million patient years of clinical experience and remains the leading hormonal therapy for new patients in the US, Japan and France. *Arimidex* is also approved in Europe for a switch indication for patients who have already received two to three years of tamoxifen.

Faslodex offers an additional hormonal therapy for patients with hormone-sensitive, advanced breast cancer, delaying the need for cytotoxic chemotherapy. *Faslodex* offers an effective, well-tolerated additional treatment with the compliance and convenience benefits of a once-monthly injection. *Faslodex* is now launched in more than 50 markets. It is approved for the second-line treatment of hormone-receptor positive, advanced breast cancer in post-menopausal women.

Casodex sales growth continued to be driven by the use of *Casodex* 50mg in advanced prostate cancer; the growth of *Casodex* 150mg, which is approved for use in locally advanced prostate cancer in over 60 countries; and the growth of *Casodex* 80mg, which is only available in Japan, where it is approved for all stages of prostate cancer.

The European Medicines Agency's Committee for Medicinal Products for Human Use reviewed the safety and efficacy of *Casodex* 150mg during 2007 and concluded in May that its benefits outweigh its risks for the treatment of locally advanced prostate cancer in patients who are at high risk of their disease getting worse.

Zoladex is used for the treatment of prostate cancer (for which it is approved in 105 countries), breast cancer and gynaecological disorders. In non-metastatic prostate cancer, *Zoladex* is the only luteinising hormone-releasing hormone (LHRH) agonist shown to improve overall survival both when used in addition to radical prostatectomy and when used in addition to radiotherapy. This was further reinforced with the publication of research in September 2007 in the journal 'Prostate Cancer and Prostatic Diseases' highlighting the value of *Zoladex* in helping prostate cancer patients outlive their disease and calling for *Zoladex* to be considered as a treatment of curative intent.

In breast cancer, *Zoladex* is widely approved for use in advanced breast cancer in pre-menopausal women. In a number of countries, *Zoladex* is also approved for the adjuvant treatment of early stage pre-menopausal breast cancer as an alternative to and/or in addition to chemotherapy. *Zoladex* offers proven survival benefits for breast cancer patients with a favourable tolerability profile.

Iressa is used for the treatment of advanced non-small cell lung cancer (NSCLC) in patients who have failed chemotherapy. Following disappointing clinical trial data in 2004 from the ISEL study, in 2005 we voluntarily withdrew the European submission for *Iressa* and the regulatory authorities in the US and Canada restricted its use to those patients already benefiting from the drug.

In the third quarter of 2007, data from the phase III international INTEREST study comparing *Iressa* with docetaxel were reported. The study met its primary objective, demonstrating equivalent overall survival for *Iressa* and docetaxel in patients with pre-treated advanced NSCLC. This is the first time that a drug in this class has shown non-inferior survival to chemotherapy in a head-to-head study in this setting. In addition, *Iressa* demonstrated a more favourable tolerability profile and superior quality of life for patients compared with docetaxel. Based on these data, we are reviewing options for possible regulatory submissions.

Iressa continues to be marketed in the Asia Pacific region for pre-treated advanced NSCLC. It is currently being investigated in the first-line advanced setting in a large, phase III, pan-Asian trial known as the IPASS study. Further phase II trials are continuing to evaluate the potential benefits of *Iressa* in NSCLC and other EGF receptor-driven tumours.

Ethyol is used to help prevent certain unwanted side effects of specific types of chemotherapies and radiotherapies that are used to treat cancer. *Ethyol* was initially approved by the US Food and Drug Administration (FDA) in 1995 to reduce cumulative (kidney) toxicity associated with repeated administration of cisplatin to patients with advanced ovarian cancer. In 1999, the FDA approved the use of *Ethyol* for the reduction of the incidence of moderate-to-severe dry mouth (xerostomia) in patients undergoing post-operative radiation treatment for head and neck cancer, where the radiation port includes a significant portion of the parotid glands. Xerostomia, both acute and chronic, is a debilitating condition in which saliva production is reduced due to damage caused to the salivary glands by therapeutic radiation. We are the sole marketer of *Ethyol* in the US. Outside the US we have various distribution and marketing arrangements for the drug. *Ethyol* has been approved for marketing in 63 countries worldwide, including the US.

Abraxane® was approved by the FDA in January 2005. It is indicated for the treatment of breast cancer after failure of combination chemotherapy for metastatic disease or relapse within six months of adjuvant chemotherapy. Our co-promotion of Abraxane® in the US under an agreement with Abraxis BioScience, Inc. commenced in July 2006. The agreement gives us access to the key US chemotherapy market and Abraxane® complements and extends our US oncology product portfolio.

PIPELINE

Zactima (vandetanib) is a potential new oral anti-cancer therapy, which has a unique profile that fights cancer through two clinically proven mechanisms. It blocks the development of a tumour's blood supply (anti-VEGFR) and blocks the growth and survival of the tumour itself (anti-EGFR). *Zactima* also inhibits RET-kinase activity, an important growth driver in certain types of thyroid cancer.

Zactima is being investigated in a number of phase III clinical trials across the world to assess its impact on survival and on the lives of patients with NSCLC and medullary thyroid cancer.

In 2005, promising early data in hereditary medullary thyroid cancer led to orphan drug designation for *Zactima* by the FDA and the European Medicines Agency, as well as fast-track status for regulatory review by the FDA. Orphan drug designation encourages the development of new products that demonstrate promise for life-threatening or very serious conditions that are rare and affect relatively few people. Fast-track designation potentially facilitates and expedites the process for the review by the FDA of new drugs intended to treat serious or life-threatening conditions and that demonstrate the potential to address unmet medical needs. A randomised phase III study of *Zactima* versus placebo in medullary thyroid cancer has completed enrolment.

In addition, the anti-cancer activity of *Zactima* continues to be evaluated in other tumour types, including colorectal, glioma, head and neck, breast and prostate cancers.

Recentin (cediranib) is a highly potent, selective, orally active inhibitor of vascular endothelial cell growth factor (VEGF) receptor signalling in solid tumours. *Recentin* inhibits all three VEGF receptors irrespective of activating ligand. Following the decision in 2005 to accelerate the development of *Recentin*, and the subsequent commencement of the pivotal phase II/III NSCLC study that year, the pivotal colorectal cancer (CRC) programme started in 2006. The CRC programme includes a head-to-head study comparing *Recentin* plus FOLFOX (a combination chemotherapy treatment made up of a number of drugs) with bevacizumab (Avastin™) plus FOLFOX in first-line treatment of CRC. It also includes two other studies in CRC, namely a second-line head-to-head study with bevacizumab and a first-line study involving *Recentin* with and without standard chemotherapy. Phase II studies of *Recentin* in gastrointestinal stromal tumours, and renal and breast cancer, are continuing. As well as these programmes, the US National Cancer Institute (NCI) is now recruiting patients for more than 15 studies in a number of different tumour settings. Encouraging data for *Recentin* from two completed NCI studies to treat renal cancer and glioblastoma were presented in 2007. The data in recurrent glioblastoma were published in the journal 'Cancer Cell' in January 2007 and presented at the American Society of Clinical Oncology meeting in June 2007. These data have led to the commencement of a development programme for *Recentin* in recurrent glioblastoma.

ZD4054 is a potent and specific endothelin A-receptor antagonist that reduces tumour growth and survival, lessening the potential for invasion and metastasis. ZD4054 entered phase III development in 2007 for patients with hormone-resistant prostate cancer (HRPC), an area of great unmet need with few treatment options.

This move into phase III development is based on promising early data from the EPOC phase II study presented at the European Congress of Clinical Oncology in September 2007. The trial suggests that ZD4054 10mg once-daily has the potential to increase the median overall survival time by approximately seven months in men with asymptomatic or mildly symptomatic metastatic HRPC, with the benefit of a generally well-tolerated side effect profile and the convenience of a once-daily tablet.

The phase III ENTHUSE global trial programme, which consists of three studies, is in the early stage of start-up and began enrolling the first patients in the fourth quarter of 2007. These trials will investigate the efficacy of ZD4054 in metastatic HRPC, both as monotherapy and in combination with docetaxel, and in non-metastatic HRPC.

Our early oncology pipeline includes novel compounds that target signalling pathways believed to be pivotal in cancer cell growth, invasion and survival, with two products in phase II and nine others in phase I development. Phase II data from AZD6244, a potent MEK inhibitor licensed from Array BioPharma, Inc., was reported in December 2007. AZD6244 showed biological activity in lung cancer and melanoma and studies will now focus on its use in combination with standard and other novel therapies, rather than its development as monotherapy. Phase II studies with the poly (ADP-ribose) polymerase (PARP) inhibitor AZD2281 have started and will initially focus on BRCA-mutated breast and ovarian cancer as well as other cancers where DNA repair could be defective.

The dual-specific Src/Abl kinase inhibitor, AZD0530, has shown a dramatic effect on biomarkers of cell motility and bone resorption and is starting phase II studies in a range of malignancies. Among the compounds from the early portfolio continuing in development are AZD4877, a novel inhibitor of cell cycle; AZD7762, a tumour-selective chemo sensitiser; and AZD8931.

MedImmune

MedImmune is developing potential new cancer treatments using biological approaches with highly defined molecular targets for patient populations with unmet medical needs.

In 2007, oncology trials underway included those for IPI-504 (also known as MEDI-561), a drug candidate designed to inhibit heat shock protein 90 (Hsp90). Hsp90 is an emerging cancer target, which is currently being evaluated as a potential treatment for three solid tumour cancers.

Development of MEDI-538, a recombinant single-chain bi-specific T-cell engager (BiTE™) molecule targeting the CD19 antigen is progressing. This candidate drug is the first and only BiTE™-inspired molecule in clinical trials, and is currently in phase I and phase II clinical development for the treatment of various B-cell malignancies. In 2007, preliminary data was released from a continuing phase I study of MEDI-538 in patients with late-stage non-Hodgkin's lymphoma.