

# '07: IN REVIEW

## The OBR Top 10 Oncology Stories of 2007

Now that 2007 has come to a close, we at OBR take a look back at some of the top stories that garnered the most media attention in '07. Feel free to visit our website at [www.oncbiz.com](http://www.oncbiz.com) and let us know if you have a different opinion.

### 1 >> Curtailing ESA Use

Erythropoiesis-stimulating agents (ESAs) were hands down the oncology story of 2007. The FDA issued a black box warning for the drugs indicating that higher doses could result in increased risk of death and accelerated tumor growth in cancer patients after studies raised safety concerns.

CMS said that they would restrict reimbursement of ESAs and recommended limiting their use. Amgen—with a huge stake in the ESA market—was enormously impacted as Aranesp® and Epogen®, the company's best-selling ESAs, were seriously affected. Johnson & Johnson's anemia-fighting drug Procrit® was also hit.

With the erosion of its key anemia franchise, which accounted for \$6.63 billion in combined sales in 2006, Amgen Chief Executive Officer Kevin Sharer announced a restructuring that would reduce global staff by up to 14 percent.

In addition, Amgen disclosed in November that the company had recently received two federal subpoenas seeking documents related to its products—details of what the prosecutors were looking for were not available in a Securities and Exchange Commission filing, but the lawsuit said that Amgen engaged in an "anticompetitive tying arrangement and pricing scheme" involving the sale of Neupogen®, Neulasta® and Aranesp.

### 2 >> FDA New Drug Approvals and Label Expansions

Although the year was marked by FDA delays and rejections of cancer drugs due to a more vigilant regulatory environment regarding safety, there were novel, and promising, anti-cancer therapies approved for difficult-to-treat cancers and patients with unmet medical needs.

#### New Drug Approvals

Roche's anemia drug, Mircera, was FDA-approved in November for the treatment of anemia that is associated

with chronic renal failure in adults, including patients who are receiving dialysis. However, sales of the drug in the US are on hold due to an ongoing patent infringement case with Amgen.

Other key FDA approvals for cancer agents were:

- Tasigna® [nilotinib; Novartis] was granted accelerated approval to treat patients with Philadelphia chromosome-positive chronic myeloid leukemia (CML) who are resistant or intolerant to existing therapies including Gleevec® [imatinib; Novartis]
- Ixempra® [ixabepilone; Bristol-Myers Squibb], a new chemotherapy treatment and one of a new class of drugs called epothilones, was approved for women with metastatic or locally advanced breast cancer who have not responded to standard chemotherapy drugs
- Tykerb® [lapatinib; GlaxoSmithKline], a once-daily pill belonging to a new class of drugs called dual-kinase inhibitors, was approved for advanced metastatic breast cancer
- Torisel® [temsirolimus; Wyeth], a targeted first-in-class mTOR inhibitor, was approved for advanced renal cell carcinoma
- Oral Hycamtin® [topotecan; GlaxoSmithKline] capsules were approved for the treatment of relapsed small cell lung cancer

#### New Label Expansions

Additional 2007 regulatory action by the FDA's Office of Oncology Drug Products (OODP) for cancer drugs included:

- Nexavar® [sorafenib; Bayer Pharmaceuticals Corp., Onyx Pharmaceuticals, Inc.], an orally-administered kinase inhibitor touted as the first approved systemic therapy for liver cancer, was approved for patients with unresectable hepatocellular carcinoma

- Sutent® [sunitinib malate; Pfizer] for first-line treatment of advanced renal cell carcinoma
- Erbitux® [cetuximab; ImClone] new labeling says that Erbitux shows improved overall survival as a single agent in colon cancer patients who have not responded to chemotherapy treatments with irinotecan and oxaliplatin
- Taxotere® [docetaxel; Sanofi-Aventis] in combination with cisplatin and 5-FU received an expansion labeling from the FDA for the treatment of locally advanced head and neck cancer for patients before treatment with chemoradiotherapy and surgery
- Evista® [raloxifene hydrochloride; Eli Lilly & Co.] won FDA approval for a new use: To reduce the risk of invasive breast cancer in postmenopausal women with osteoporosis and in postmenopausal women at high risk for invasive breast cancer
- Sprycel® [dasatinib; Bristol-Myers Squibb] new labeling includes a lower recommended starting dose of 100 mg once daily in patients with chronic-phase CML who are resistant or intolerant to prior therapy including Gleevec. The product labeling also includes data from the first randomized trial comparing Sprycel and Gleevec

### 3 >> Cancer Deaths Decline in the US

At the beginning of the year, the American Cancer Society reported that the number of Americans dying from cancer had declined for the second year in a row. Researchers attributed much of the decrease to smoking cessation and improved detection and treatment of colorectal, breast, and prostate cancers.

Deaths from colorectal cancer showed the greatest decline with rates dropping 5.7 percent—primarily due to increased screenings and improved treatment. Breast cancer incidence, which had climbed for decades, leveled off, the report said, due to both a drop in the use of hormone replacement therapy and increased rates of mammography. [cont. on pg 32 >>](#)

## The OBR Top 10 Deals of 2007

We saw a lot of activity in the deal making segment of the oncology industry last year. Perhaps it was because IMS is forecasting sales of oncology products to increase to \$60 billion by 2010. See below for some of the more notable transactions in '07.

RANK	DEAL
01	AstraZeneca's immediate payoff to its \$15.6 billion all-cash purchase of MedImmune may be infectious disease drugs, but the real reason the company is paying 53 percent more than what analysts say MedImmune is actually worth is because of its early-stage pipeline of cancer drugs. The companies recently established a joint R&D executive committee to maximize their respective drug discovery efforts. (Announced: April 23, 2007)
02	In a bid to become a global marketer of blood cancer drugs, Celgene Corp. announced that it will acquire rival Pharmion Corp. in a \$2.9 billion cash and stock transaction, or \$72 per share. With the buy-out, Celgene acquires Vidaza® and regains worldwide rights to Thalomid®, which Pharmion planned to sell at deep discount to Celgene's Revlimid®. (Announced: November 18, 2007)
03	In a \$3.9 billion cash transaction intended to strengthen its global oncology business, Tokyo-based Eisai Co. announced plans to buy MGI Pharma Inc. A Thomas Weisel Partners analyst predicted that the Eisai/MGI merger could split the US myelodysplastic syndromes (MDS) market—Pharmion has blood cancer treatment Vidaza®, which is similar to MGI's Dacogen®. MGI's other marketed products include Gliadel Wafer®, used to treat brain tumors, and Aloxi®, which treats chemotherapy-induced nausea. (Announced: December 10, 2007)
04	Small biotech Synta Pharmaceuticals Corp. cinched a deal worth up to \$1.1 billion with GlaxoSmithKline for joint development and commercialization of the experimental drug elesclomol (formerly STA-4783) for advanced melanoma, with potential for broader indications. Synta received an initial \$80 million upfront cash payment in December from GSK. The drug, a first-in-class, small-molecule, oxidative stress inducer, is currently in a pivotal Phase 3 trial for metastatic melanoma. (Announced: October 10, 2007)
05	Ariad Pharmaceuticals Inc. signed a global deal, valued at up to \$1 billion, with Merck & Co. Inc. to collaborate on developing and commercializing deforolimus. Initially being tested in sarcomas, analysts see long-term potential in the mTOR inhibitor for a broad range of cancers. The deal is unique because Ariad will market the drug itself to US oncologists, with Merck selling to doctors overseas. (Announced: July 12, 2007) <a href="#">cont. on pg 32 &gt;&gt;</a>

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The report also highlighted that several population groups within the US, such as the poor, those lacking insurance or access to medical care, or those with lower levels of education are not benefiting from the same reduction in cancer incidence as the rest of the population.

## 4 ➤ The Threat of Follow-On Biologics

Throughout 2007, but especially in the first half of the year, there was recurring debate in Congress about creating a legislative pathway for approval of biologics used to treat cancer and other diseases. Those opposed argue that manufacturing biologics requires technology that cannot be reproduced by generic manufacturers—placing patients at risk while decreasing incentive for innovation. Advocates say that manufacturing can be done in a safe manner, and that expedited clinical trials can establish safety and effectiveness. In India, Dr. Reddy's Laboratories began marketing a generic version of Rituxan® at half the cost of the original drug. Either way, legislation for follow-on biologics was not approved, but will remain in the forefront for 2008.

## 5 ➤ Setbacks in Prostate Cancer

In other immunotherapy news, Dendreon saw its stock soar to new highs with the anticipated approval of Provenge®—its immunotherapy against prostate cancer—then plunge when the FDA decided it needed further proof of efficacy—which could take up to 3 years to provide. The FDA was criticized for allowing other products on the market without long-term safety follow up. With so few options available for the treatment of prostate cancer, critics say the FDA is being too strict in making overall survival the hurdle for approval of cancer drugs.

Patients with prostate cancer had another hope for a treatment choice in July 2007 when GPC Biotech's satraplatin was reviewed by ODAC. However, after the negative outcome, the company withdrew their NDA and subsequently GPC Biotech stock plummeted. The company received more bad news in October when results from a pivotal Phase 3 trial showed that satraplatin didn't help patients live longer, putting an end to hope for a new hormone refractory prostate cancer therapy in 2007.

## 6 ➤ Cancer Vaccine Controversy

Gardasil® had its share of controversy in 2007. Merck & Company scored a big hit in the cancer headlines with the FDA approval of the vaccine in June 2006 to prevent cervical cancer and/or genital warts caused by strains of the human papillomavirus (HPV)—a sexually transmitted disease. With the CDC reporting that HPV is the most common STD in the US and with more than 80 percent of women estimated to acquire the virus by age 50, several school districts across the country announced they would be vaccinating their female student population. The vaccine is approved for girls and women ages 9 to 26.

The approval opened up a sociological discussion on how widespread the use of the vaccine should be, who should be vaccinated, and when. Parents were angered over the thought of their pre-teen daughters getting vaccinated for an STD, and other moral protagonists felt the vaccine would encourage promiscuity among teenagers. Merck is seeking to expand the use of the drug for protection against vaginal and vulvar cancers, in addition to broadening its use for women up to age 45.

## 7 ➤ The High Price of Cancer Drugs

Throughout 2007 there was continuing criticism of the high cost of all drugs, and cancer drugs, whose cost increased 27 percent in 2006, seemed to take the lion's share of the spotlight. Drug companies continued to reiterate that prices reflected the cost of cancer drug innovation and investment in research and development. Two of the industry's most high-profile companies, Amgen and Genentech, responded to the criticism by instituting pricing caps.

Amgen announced a "cap" on the cost of Vectibix™ in late 2006 at \$55,000/year; Genentech followed suit shortly thereafter and launched its own "cap" on the cost of Avastin®, also at \$55,000/year, in early 2007.

The public's perception of a highly profitable industry with a sometimes questionable cost/benefit ratio for products seemed to gain momentum along with questionable promotional tactics such as DTC advertising and conflicts of interest between industry and physicians.

## The OBR Top 10 Deals of 2007 (cont.)

RANK	DEAL
06	In a potential \$890 million deal, Novartis AG licensed exclusive worldwide rights for vascular disrupting agent AS404 (formerly AS1404) from London-based Antisoma PLC after early tests showed promise in lung cancer. The companies plan to challenge Avastin®, an established blockbuster in the lung cancer market—Antisoma has enlarged studies for AS404 in both major types of NSCLC with hopes to expand the drug's market potential. Antisoma already collected a \$75 million payment from Novartis in September. (Announced: April 19, 2007)
07	GlaxoSmithKline (GSK) and privately held OncoMed Pharmaceuticals Inc. signed a deal giving GSK access to OncoMed's antibodies targeting cancer stem cells. In addition to an undisclosed upfront payment and equity investment from GSK, OncoMed could earn up to \$1.4 billion in milestones. The collaboration gives GSK an option to license four product candidates from OncoMed's library of monoclonal antibodies and yet again increases their presence in oncology. (Announced: December 10, 2007)
08	Seattle Genetics's (SGEN) shares jumped 28 percent after an exclusive worldwide licensing agreement with Genentech to develop and market blood cancer drug SGN-40 was announced. SGEN already received an upfront payment of \$60 million in February, and in December initiated a Phase 2b trial of SGN-40 as a combination cancer therapy in lymphoma, which triggered a \$12 million milestone payment from its partner. SGEN has the potential to receive milestone payments exceeding \$800 million in the deal and escalating double-digit royalties starting in the mid-teens. (Announced: January 8, 2007)
09	Sanofi-Aventis SA expanded its stake in Regeneron Pharmaceuticals Inc. to 19 percent, gaining non-exclusive access to Regeneron's proprietary VelociSuite of technologies for the development and commercialization of fully-human therapeutic antibodies. Sanofi will pay \$85 million upfront and up to \$475 million to Regeneron over the next five years. Regeneron entered into similar agreements with AstraZeneca and Astellas Pharma earlier in 2007, licensing its VelocImmune® technology platform for the same purpose. (Announced: November 29, 2007)
10	With an eye on enhancing its specialty drugs business in oncology, mega-drug wholesaler McKesson Corp. acquired Oncology Therapeutics Network, one of the largest cancer drug distributors in the US, for about \$575 million, including debt. The deal closed October 29, just before McKesson announced second-quarter earnings. (Announced: October 4, 2007) <b>OBR</b>

### 8 >> Personalized Medicine

A recurring theme coming out of ASCO 2007 was the move toward using genetic testing to tailor cancer therapies to the individual patient. Cancer researchers are hoping to use gene sequencing to learn what went wrong in the DNA of tumor cells, and drug companies are hoping to capitalize on knowledge of the genome to develop custom-made therapies based on gene sequencing. The success in the marketplace for genetic breast cancer tests, such as Genomic Health's Oncotype DX® and Agendia's MammaPrint®, which captured a TIME Magazine award as one of the best inventions of '07, demonstrates the enthusiasm for this category.

### 9 >> ASCO Changes Annual Meeting Policy

After years of criticism, ASCO decided to change a long-standing policy by posting annual meeting research abstracts on its website, and making them available to everyone. Critics have been campaigning for ASCO to change its policy for years, complaining that by not making abstracts public they were allowing ASCO members exclusive access to potentially market-moving information. ASCO will post abstracts on their website approximately 2 weeks prior to the next annual meeting in 2008.

### 10 >> The American Cancer Society's New Awareness Campaign

The organization decided to take a different approach to advertising in 2007 and is going to spend their entire \$15 million advertising budget on a new campaign highlighting the consequences of inadequate health coverage for Americans with cancer. The announcement created debate because many thought that the ACS should be raising awareness for cancer prevention and early detection, not spending valuable resources on the broader issue of lack of insurance coverage for cancer patients. ACS's Chief Executive Officer, John R. Seffrin said that advances in prevention and research would have little impact if Americans couldn't afford cancer screening and treatment. **OBR**