THE TOOLS

[Approved Drugs]

■ Genentech, Inc. (South San Francisco, Calif.) announced that the Food and Drug Administration (FDA) has approved **Avastin® (bevacizumab)** to be used in combination with carboplatin and paclitaxel chemotherapy for the first-line treatment of patients with unresectable, locally advanced, recurrent or metastatic, non-squamous, non-small cell lung cancer. The approval is based on a Phase III study (E4599) that showed Avastin in combination with chemotherapy resulted in a 25 percent improvement in overall survival compared to chemotherapy alone.

■ Cephalon, Inc. (Frazer, Penn.) has received approval from the FDA to market **Fentora™ (fentanyl buccal tablet) [C-II]** for the management of breakthrough pain in patients with cancer who are already receiving and who are tolerant to opioid therapy for their underlying persistent cancer pain. Fentora is the first and only buccal tablet approved for this indication.

With Fentora's drug delivery technology, approximately half of the medicine is absorbed directly across the lining of the upper cheek, the buccal mucosa, and into the bloodstream more quickly than if it were swallowed and broken down by the liver in the gastrointestinal tract.

Cephalon will manufacture Fentora in five dosage strengths: 100, 200, 400, 600, and 800 micrograms.

■ The FDA has approved two additional uses for **Rituxan® (rituximab)** (Genentech, South San Francisco, Calif., and Biogen Idec, Cambridge, Mass.) for patients with CD20-positive, B-cell non-Hodgkin's lymphoma (NHL). The first new indication is for first-line treatment of previously untreated patients with follicular NHL in combination with CVP (cyclophosphamide, vincristine, and prednisolone) chemotherapy. The second new indication is for the treatment of low-grade NHL in patients with stable disease or patients who achieve a partial or complete response following first-line treatment with CVP chemotherapy.

■ Cytogen Corporation (Princeton, N.J.) announced that **Soltamox™ (tamoxifen citrate, oral solution 10mg/5mL),** the first liquid form of the hormonal breast cancer therapy tamoxifen, is currently being introduced in the United States and is available in U.S. pharmacies nationwide. Soltamox received FDA marketing approval in October 2005 and is indicated for the treatment of metastatic breast cancer and to reduce the incidence of breast cancer in women who are at risk for the disease.

■ **Vectibix™ (panitumumab)** has received FDA approval for the treatment of advanced colon cancer with patients whose colon cancer has spread after chemotherapy has failed.

Vectibix (Amgen Inc., Thousand Oaks, Calif.) is the first entirely human monoclonal antibody for the treatment of patients with epidermal growth factor receptor- (EGFr) expressing metastatic colorectal cancer after disease progression on, or following fluoropyrimidine-, oxaliplatin-, and irinotecan-containing chemotherapy regimens.

FDA approval was based on a pivotal-stage trial that showed that patients treated with Vectibix showed a better-than-expected 46 percent decrease in the rate of tumor growth versus those who received supportive care. Vectibix is the first anti-EGFr antibody shown to significantly improve progression-free survival in patients with metastatic colorectal cancer.

As part of the approval, Amgen will conduct a post-marketing trial to show whether the drug improves patients' survival in patients with fewer prior chemotherapies.

[Drugs in the News]

■ The FDA has granted orphan drug designation to **Atiprimod** for the treatment of carcinoid tumors. Atiprimod is a small molecule antiangiogenic drug that is being developed by Callisto Pharmaceuticals, Inc. (New York, N.Y.) to treat advanced carcinoid tumors, as well as relapsed multiple myeloma patients. Callisto plans to begin a Phase II clinical trial in advanced carcinoid cancer patients in the coming months.

■ MGI Pharma (Minneapolis, Minn.) announced that the FDA has granted **Dacogen™ (decitabine) for injection** orphan drug designation for the indication of acute myeloid leukemia. Dacogen is a hypomethylating agent that is believed to exert its antioneoplastic effects by incorporation into DNA and inhibition of an enzyme called DNA methyltransferase.

■ The FDA has granted orphan drug designation to Threshold Pharmaceuticals, Inc.'s (Redwood City, Calif.) product candidate, **glufosfamide**, for the treatment of pancreatic cancer.

Last month the company announced that it had completed enrollment in a pivotal Phase III clinical trial evaluating glufosfamide for the potential second-line treatment of pancreatic cancer and a Phase II clinical trial evaluating glufosfamide in combination with gemcitabine for the potential first-line treatment of pancreatic cancer. Top-line results from both of these clinical trials are expected by the end of 2006.

■ The FDA has granted priority review to Millennium

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Fast Facts

Adverse Drug Events and Our Seniors

- Patients over 65 years of age consistently experience a drug error rate approximately 7 times greater than patients younger than 65
- Seniors seeing five doctors have a 60 percent greater risk of adverse events over those seeing only two physicians
- One in four seniors receive prescriptions from five or more doctors; one in 20 receive prescriptions from eight or more physicians
- Nearly 25 percent of seniors fill their prescriptions at three or more pharmacies

Source: Medco Health Solutions, Inc., 2006. An analysis of 2004 prescription drug claims.

Pharmaceuticals, Inc.'s (Cambridge, Mass.) supplemental new drug application (sNDA) for **Velcade® (bortezomib) for Injection** for treatment of relapsed mantle cell lymphoma.

The sNDA submission was based on final Phase II data from the PINNACLE study, which showed a 33 percent overall response rate and an 8 percent complete response rate. Importantly, the median duration of response was 9.2 months, and 13.5 months in patients who achieved a complete response. These results are similar to those of four investigator initiated Phase II clinical trials where overall response rates of 30 to 40 percent with single-agent Velcade were established.

■ Exelixis, Inc. (South San Francisco, Calif.) has submitted an investigational new drug application (INDA) to the FDA for **XL228,** a novel anticancer compound designed to inhibit the insulin-like growth factor type-1 receptor (IGF1R), Src and Abl tyrosine kinases. These targets play crucial roles in cancer cell proliferation, survival, and metastasis. XL228 is a potent inhibitor of the T315I mutant form of the Abl protein, which is associated with resistance to currently approved therapies. Phase I clinical trials of XL228 are expected to be initiated in the fourth quarter of 2006.

[Devices in the News]

■ Amgen announced the launch of the **Aranesp® (darbepoetin alfa) prefilled SureClick™ autoinjector** for patients with chemotherapy-induced anemia and anemia associated with chronic kidney disease. The prefilled autoinjector includes a safety cover that limits needle exposure before and after the subcutaneous injection, two audible clicks to announce the beginning and end of the injection, and a large inspection window that confirms it automatically delivered the complete injection.

■ Abbott (Abbott Park, Ill.) announced FDA 510(k) clearance for **Cell-Dyn Ruby™,** the company's automated, mid-volume hematology instrument. The device uses laser light to differentiate cellular components. This all-optical technology provides detailed results in easy-to-view diagrams, visually depicting changes in white and red blood cells and platelets.

■ Calypso Medical Technologies, Inc. (Seattle, Wash.) announced that the FDA has granted 510(k) clearance for the **Calypso® 4D Localization System**, which is designed to enable clinicians to measure and monitor organ motion during radiation therapy for cancer patients. Because the product platform does not require expertise in interpreting x-ray or ultrasound images, it greatly reduces the time to perform patient setup, a well-recognized bottleneck in the radiation department workflow.

■ Endocare, Inc. (Irvine, Calif.) announced that the company has received 510(k) clearance from the FDA to market its new **Cryocare CN2 System.** This new system uses nitrogen as the freezing and tumor-destroying element. The nitrogen, called "critical nitrogen" because it works in a unique form at the critical point where gas nearly becomes liquid, is more powerful and more readily available in surgical suites than argon, the freezing element in Endocare's current cryoablation systems.

■ Elekta (Stockholm, Sweden) announced that the FDA has granted 510(k) pre-market clearance for **Leksell Gamma Knife® Perfexion™**, a new stereotactic radiosurgery system that is designed to maintain full clinical compatibility with Gamma Knife procedures and protocols. The new system comes with Leksell GammaPlan® PFX™, a new client-based treatment planning system with remote capabilities. Leksell GammaPlan PFX received FDA clearance in July 2006.

■ Focus Surgery, Inc. (Indianapolis Ind.) announced that the FDA has granted a provisional investigational device exemption (IDE) for its **Sonablate® 500,** which will allow the device to be used in a multi-center clinical study to collect safety and efficacy data for final FDA approval. The Phase III clinical study will use high-intensity focused ultrasound (HIFU) in conjunction with the Sonablate® 500 for the treatment of low-risk, localized (T1c/T2a) prostate cancer. The study will enroll approximately 466 subjects at 24 institutions.

HIFU is a targeted, precise treatment that uses sound waves to rapidly heat and kill targeted tissue while sparing the surrounding tissue. The Sonablate® 500-HIFU device uses real-time ultrasound image guidance for the treatment of prostate cancer. This non-invasive procedure is performed on an outpatient basis and international studies suggest a substantial reduction in common side effects such as impotence and incontinence.