TREANDA Significantly Improves Clinical Outcomes in Patients with Chronic Lymphocytic Leukemia Compared to Chlorambucil in Phase III trials

Cephalon, Inc. (NASDAQ:CEPH) announced that in a pivotal study of treatment-naive patients with chronic lymphocytic leukemia (CLL), those who received TREANDA (bendamustine HCl) had better clinical outcomes compared to patients treated with chlorambucil, an FDA-approved therapy for patients with CLL. TREANDA(R) is a novel investigational chemotherapy that is currently under priority review by the USFDA. CLL is a slowly progressing blood and bone marrow disease with an estimated 15,000 new cases diagnosed every year in the US, according to the National Cancer Institute.

Source: Adis Insight

A Promising New Drug Target for Angiogenesis Inhibition

VEGF-targeted therapies, approved recently for the treatment of colorectal, lung, renal and hepatocellular cancers, either prolong survival by few months and/or delay the progression of the disease. Tumors ultimately develop resistance to these agents by up-regulating other angiogenic factors. VEGF inhibition is also associated with serious adverse events in a few patients. An agent that blocks angiogenesis, tumor growth and metastasis without serious toxicities is highly desirable.

In the November issue of Cell, Peter Carmeliet and his colleagues described the potential of neutralizing antibodies against placental growth factor (PGF), a VEGF homologue, as an anti-angiogenic agent. Their studies showed that anti-PGF antibodies inhibited tumor growth in 12 different mouse models, including the VEGF-resistant tumors, and enhanced the efficacy of chemotherapy. Interestingly, anti-PGF antibodies did not elicit the adverse toxicities associated with VEGF inhibition. These data indicate that PGF inhibition is a promising therapeutic strategy for inhibiting tumor growth and metastasis.

Source: Cell, Nov. 2007

GlaxoSmithKline’s Tyverb Receives Positive Opinion in EU

On December 13, 2007, CHMP adopted a positive opinion for the medicinal product Tyverb, 250 mg, intended for the treatment of patients with advanced or metastatic breast cancer whose tumors over express ErbB2 (HER2) and who have received prior therapy, including anthracyclines, taxanes, and trastuzumab …more on Pg-3

Avastin, Xeloda and MabThera Receive Positive Opinions from EU Committee

Roche reported that it received positive opinions from the EU’s CHMP, which recommended labeling extensions for both Xeloda and Avastin for the treatment advanced colorectal cancer. Additionally, the CHMP recommended expanded approval for MabThera in the treatment of previously untreated patients with stage III-IV follicular lymphoma in combination with chemotherapy…more on Pg-3
**Clinical Development**

**Phase III Trial Reports Revlimid® Plus Dexamethasone Achieves Superior Progression-Free Survival in Newly Diagnosed Multiple Myeloma Patients**

Celgene International Sàrl (NASDAQ: CELG) presented final results from the Southwest Oncology Group’s (SWOG) Phase III randomized, controlled trial evaluating the combination therapy of Revlimid and Dexamethasone in patients with newly diagnosed multiple myeloma, at the ASH-2007 meeting. There was 77% one-year, progression-free survival in Revlimid plus Dexamethasone arm compared to 55% for Dexamethasone alone. The overall response rate was 85% with Revlimid plus Dexamethasone compared to 51% in Dexamethasone alone. "These results demonstrate that Revlimid plus Dexamethasone is an excellent treatment in newly diagnosed multiple myeloma," said Dr. Durie (co-chairman of the SWOG Myeloma Committee).

*Source: SECinfo*

**Roche’s MabThera Improves Response in Patients with CLL**

Roche presented early results from two Phase II trials, demonstrating the efficacy of MabThera in CLL patients, at the ASH-2007 meeting. In the first trial, 92% patients, with previously untreated CLL, responded to treatment with MabThera in combination with chemotherapy. The study is also investigating the impact of MabThera maintenance therapy in CLL patients. Further results from the second part of the study are expected in 2008. The second trial focused on patients with relapsed CLL and demonstrated a better response for patients treated with MabThera in combination with chemotherapy (70%) than with chemotherapy alone (57%). "These early results seem to signify that the addition of MabThera to treatment is critical to improving outcomes in CLL patients, where there is currently a high unmet medical need" said Prof. Emili Montserrat from the Department of Hematology in University of Barcelona, Spain.

*Source: Roche*

**Dasatinib, Nilotinib Show Strong Early Results as Frontline Therapy for Chronic Myelogenous Leukemia**

Research teams led by scientists at The University of Texas M. D. Anderson Cancer Center reported, at the 49th annual ASH meeting, that two drugs approved for use as second-line therapy for chronic myelogenous leukemia are showing promising results as frontline therapy for the newly diagnosed patients in two clinical trials. "These are early results but certainly encouraging so far in both cases," said lead author Jorge Cortes, M.D., professor in M. D. Anderson’s Department of Leukemia. Patients in both trials are in the chronic or initial phase of CML and have not received prior therapy for the disease. The two medications are dasatinib, the Bristol-Myers Squibb’ drug, Sprycel, and nilotinib, the Novartis’ drug, Tasigna. Both have been approved by the US FDA for use in CML patients who become resistant to imatinib - the frontline therapy which is also a Novartis drug known as Gleevec, or become intolerant to the drug.

*Source: MD.Anderson*

**Research Highlights**

**Essential Role of Heat Shock Response in Tumorigenesis**

Heat shock response protein 90 (HSP90) can promote the folding of damaged proteins. Inhibition of the ATPase activity of HSP90 results in the depletion of HSP90 client proteins, particularly kinases that are involved in signal transduction and oncogenesis. These inhibitors target the HSP90 complexes present in cancer cell but not in normal cells. A recent study published in *Cell* by Dai et al. showed that heat shock response plays an essential role in initiating and maintaining tumorigenesis. The study demonstrated that knocking out heat shock factor-1 (HSF-1), which regulates the transcription of heat shock proteins, in mice—also in mice with germ line p53 mutations—prevented them from developing tumors induced in the skin carcinogenesis model. These studies show that HSF-1, although not an oncogene, is important for tumorigenesis.

*Source: Cell Dec. 2007*

**Linking Retinoic Acid (RA) Pathway and Histone Deacetylase Inhibitors**

The exact mechanism by which histone deacetylase inhibitors (HDACIs) induce apoptosis and anti-tumor effects is not well understood. Rene Bernards and his colleagues used functional genetic screens to identify pathways that confer resistance to HDACIs. They showed that expression of retinoic acid receptor-alpha (RAR-alpha) and the preferentially expressed antigen of melanoma (PRAME), which is a repressor of RA signaling, conferred resistance to HDACIs in tumor cells. HDACIs were found to induce RAR-alpha transactivation, suggesting that de-repression of RA pathway is one mechanism by which these inhibitors exert their anti-tumor activity. The authors concluded that RA pathway is a rate-limiting target of HDACIs.

*Source: P.N.A.S Dec. 2007*

**Cancer-associated Genes in Breast and Colorectal Cancers**

A large number of oncogenes and tumor suppressor genes have been identified in the last two decades. Recent studies from Bert Vogelstein’s lab showed that many more cancer-associated genes remain to be discovered. His group sequenced all the reference genes in the human genome database, from 11 breast and 11 colon tumor samples, and analyzed the non-silent mutations to identify 280 cancer-associated genes. Mutations affecting the PI-3 kinase/AKT pathway were particularly common, although different parts of the pathway were mutated in breast and colorectal tumors.

*Source: Science, Nov. 2007*

**The Extra cellular Matrix Protein TGFBI Induces Microtubule Stabilization and Sensitizes Ovarian Cancers to Paclitaxel**

The extra cellular matrix (ECM) can induce chemotherapy resistance through AKT-mediated inhibition of apoptosis. In the cancer cell article, it is shown that the loss of the ECM protein, TGFBI (transforming growth factor beta induced), is sufficient to induce specific resistance to paclitaxel and mitotic spindle abnormalities in ovarian cancer cells. Paclitaxel-resistant cells treated...
with recombinant TGFBI protein show integrin-dependent restoration of paclitaxel sensitivity through FAK- and Rho-dependent stabilization of microtubules. Immunohistochemical staining for TGFBI in paclitaxel-treated ovarian cancers from a prospective clinical trial showed that morphological changes of paclitaxel-induced cytotoxicity were restricted to areas of strong expression of TGFBI. These data show that ECM can mediate taxane sensitivity by modulating microtubule stability.

Source: Cancer cell. Dec. 2007

Panel of Serum Biomarkers for the Diagnosis of Lung Cancer

No blood test for lung cancer is available and serum biomarkers that can aid clinicians in making case management decisions will be extremely valuable for the detection of lung cancer. In a study published in JCO, four serum proteins—carcinoembryonic antigen, retinol binding protein, α1-antitrypsin, and squamous cell carcinoma antigen—were collectively found to correctly classify the majority of lung cancer. The markers distinguished lung cancer patients from control patients with 77.8% sensitivity and 75.4% specificity, reported Edward F. Patz, Jr., M.D., and colleagues at Duke University. A classification and regression tree model (CART), based on samples from 50 patients and 50 controls, determined the levels of these markers, in various combinations, that can best distinguish lung cancer patients from age- and sex-matched controls. This panel of four serum proteins is valuable in suggesting the diagnosis of lung cancer, particularly for treating patients with an indeterminate pulmonary lesion and for identifying individuals at high risk for lung cancer.


Regulus Therapeutics and Collaborators Discover Role of Viral microRNAs in Cancer

MicroRNAs, a recently discovered class of genetically encoded small RNAs, represent a new approach for the treatment of a wide range of human diseases—including cancer, viral infection, and metabolic disorders. A study, performed by Regulus Therapeutics (a joint venture between Alnylam Pharmaceuticals, Inc. and Isis Pharmaceuticals, Inc.) in collaboration with scientists from Duke University, shows that a virally derived microRNA mimics the gene expression control by an endogenous host microRNA that has previously been implicated in human cancer. The study shows that a viral microRNA miR-K12-11, which is encoded by KSHV, functions as a mimic of the host cell microRNA, known as miR-155. Expression of physiological levels of miR-K12-11 or miR-155 was found to result in the down-regulation of an extensive set of common mRNA and protein targets, including genes with known roles in cell growth regulation. Considering the important role of miR-155 in cancer and B-cell function as well as the association of KSHV infection with B-cell lymphomas and Kaposi’s sarcoma, miR-K12-11 may represent the first example of a viral "oncomir."

Source: Nexis

New Cancer Drug Tied to Heart Problems

A study finds that sunitinib (Sutent), the new and powerful cancer drug which fights stomach tumors, can also create heart problems for some patients. The new, collaborative study, which is published in the December 15 issue of The Lancet, was supported by Children’s Hospital Boston; the Dana-Farber Cancer Institute; Thomas Jefferson University; the US National Heart, Lung, and Blood Institute; the Finnish Heart Foundation; and the American Heart Association. All patients taking sunitinib, but especially those who are at risk for heart disease are at greater risk, require careful monitoring and treatment for high blood pressure and other signs of heart problems, researchers say.

Source: The Lancet; Dec. 15, 2007

Avastin, Xeloda and MabThera Receive Positive Opinions from EU Committee

Regarding Xeloda, the committee recommended that the drug should be made available in the EU to treat metastatic colorectal cancer in combination with other chemotherapies. Avastin was granted a positive opinion for use in combination with Xelox or FOLFOX-4, for patients with metastatic advanced colorectal cancer.

Source: EMEA

Genzyme Thyroid Cancer Drug Gets Broader US Use

Genzyme Corp., on Monday, said that the US FDA approved a broader use of Thyrogen, the thyroid cancer treatment. The new indication will extend use of the drug to patients, earlier in their treatment for thyroid cancer, the Cambridge, Massachusetts-based biotech said. The drug can now be used in combination with radioactive iodine to kill remaining thyroid tissues after patients have had cancerous thyroids removed. Approximately 33,550 new cases of thyroid cancer are expected to be diagnosed in 2007 in the US, the company said, citing the American Cancer Society.

Source: EMEA

Amgen's Vectibix Granted Conditional EU Approval in Second-line mCRC

The European Commission has granted a conditional marketing approval to Vectibix...
(panitumumab) as monotherapy, for the treatment of patients with epidermal growth factor receptor (EGFR) expressing metastatic colorectal cancer (mCRC) with non-mutated (wild-type) KRAS genes after the failure of standard chemotherapy regimens. The approval is based on a positive benefit/risk assessment in a patient population that has few treatment options available. The phase III clinical trial demonstrated that the effect of Vectibix on progression-free survival (PFS) was confined exclusively to the approximately 60% patients whose tumors harbor normal, non-mutated (wild-type) KRAS. Vectibix had no clinical benefit in patients who had tumors with mutations in KRAS, regardless of the endpoint studied. Vectibix was approved for use by the US FDA in September 2006.

Source: EMEA

**FDA Wants More Info on Cervical-Cancer Vaccine Cervarix**

The US FDA seeks more information on GSK’s cervical-cancer vaccine Cervarix before clearing it for marketing. GSK did not say what questions were asked, other than to note that the talks were ‘positive and constructive.’ The vaccine is already approved in 45 countries, including the 27 member countries of the European Union as well as Mexico and Australia. Glaxo’s vaccine competes with Merck’s MRK Gardasil, which has been available for a year in the US. It is prescribed for use by females aged 9 to 26.

Source: MarketWatch

**FDA Grants Celldex's CDX-110 Orphan Drug Status for Glioblastoma Multiforme**

The FDA has granted an orphan drug designation to Celldex’s CDX-110 for the treatment of Glioblastoma Multiforme (GBM). GBM is the most common and aggressive form of brain cancer. CDX-110 is a novel EGFR-III vaccine for Glioblastoma Multiforme. In the ACTIVATE Phase IIa study, patients treated with CDX-110 showed a median survival time of 30 months, representing more than a 100 percent increase in survival.

Source: Thomson Pharma

**Business News**

**GlaxoSmithKline and OncoMed Pharmaceuticals form Strategic Alliance**

GlaxoSmithKline (GSK) and OncoMed Pharmaceuticals (OncoMed) announced a worldwide strategic alliance to discover, develop, and market novel antibody therapeutics to target cancer stem cells, which are believed to play a key role in the establishment, metastasis, and recurrence of cancer. The alliance with GSK will be conducted through its Center of Excellence for External Drug Discovery (CEEDD). The alliance leverages OncoMed’s expertise in the discovery and development of cancer stem cell antibody therapeutics. It also provides GSK with an option to license four product candidates directed at multiple cancer stem cell targets from OncoMed’s broad library of monoclonal antibodies. OncoMed will receive an undisclosed initial payment comprising cash as well as an equity investment. In addition, OncoMed is eligible to earn milestone payments of up to $1.4 billion from GSK, based on the achievement of specified discovery, development, regulatory, and commercial milestones.

Source: GSK

**Eisai Gaining Cancer Portfolio in $3.9B MGI Acquisition**

MGI Pharma Inc. agreed to be acquired by Eisai Co. Ltd. for $41 per share, or nearly $3.9 billion in cash. The company said in its press release that if a better offer comes along, MGI can back out by paying Eisai a $129 million break-up fee. For Tokyo-based Eisai, the acquisition of MGI is one of the several recent moves to grow its US oncology franchise. Earlier this year, Eisai bought Exton, Pa.-based Morphotek Inc. for its clinical-stage anticancer antibody program. Last year, it also bought three marketed cancer drugs from Ligand Pharmaceuticals Inc. The MGI deal adds five more marketed cancer products to the mix: Aloxi (palonosetron hydrochloride), for chemotherapy-induced nausea and vomiting (CINV); Dacogen (decitabine), for myelodysplastic syndromes (MDS); Gliadel Wafer (polifeprosan 20 with carmustine implant), formalignant gliomas; Hexalen (altretamine), for ovarian cancer; and Salagen (pilocarpine hydrochloride), for dry mouth associated with Sjogrens Syndrome and radiation therapy.

Source: Eisai

**Celgene to Acquire Pharmion for $2.9 Billion in Cash and Stock**

Celgene Corporation and Pharmion Corporation jointly announced the signing of a definitive merger agreement, under which Celgene will acquire 100% outstanding common stock of Pharmion for $72 per share, payable as a combination of cash and shares of Celgene’s common stock. The acquisition of Pharmion furthers Celgene’s strategy to become a global leader in the hematologic/oncology field. Pharmion has four products on the market and several in development, all of which focus on hematological and solid tumor cancers. The transaction brings together three medically significant therapies: Revlimid, Thalomid (for multiple myeloma), and Vidaza (for myelodysplastic syndromes)

Source: Pharmion

**Center for Molecular Medicine (CMM) Among First Lab to Offer Groundbreaking Test to Aid in Treatment of Colorectal Cancer (CRC)**

The CMM is offering the Cell Search System to physicians as a vital new tool in managing patients with metastatic CRC (also called stage IV or advanced). The Cell Search System is the first diagnostic test to identify and count circulating tumor cells (CTCs) that detach from solid tumors, enter the bloodstream, and predict progression-free and overall-survival in patients, earlier than the current standard of care. The system’s specificity, sensitivity, and reproducibility allow assessment of CTCs as early as the first cycle of treatment to help evaluate disease progression sooner.

Source: Nexis

**Otsuka Pharmaceutical Acquires Rights to IV Busulofex from PDL BioPharma**

Otsuka Pharmaceutical Co., Ltd. (OPC) and PDL BioPharma, Inc. (NASDAQ: PDLI) announced that they have entered into a definitive agreement, under which Otsuka will acquire, from PDL, the rights to IV

Source: OncoMed Pharmaceuticals form Strategic Alliance

Groundbreaking Test to Aid in Treatment of Colorectal Cancer (CRC)

**FDA**

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Groundbreaking Test to Aid in Treatment of Colorectal Cancer (CRC)
Busulfex (busulfan), including trademarks, patents, intellectual property, and related assets, for $200 million, to be paid in cash at closing. IV Busulfex is an oncologic product marketed and sold by PDL in the US, Canada and over 40 countries worldwide. It is the only drug that is FDA-approved for use in combination with cyclophosphamide as a conditioning agent in allogenic hematopoietic stem cell transplantation for CML.

Source: Otsuka

Oasmia Pharmaceutical Announces Licensing Agreement with Orion Corporation Regarding New Innovative Ovarian Cancer Drug Candidate, Paclical

Oasmia Pharmaceutical (Sweden) and Orion Corporation (Finland) have entered a license and distribution agreement for marketing and sales of Paclical (micellar paclitaxel), the human cancer drug, in the Nordic region, encompassing Sweden, Denmark, Norway, Finland, and Iceland. Paclical is entering into clinical phase III with ovarian cancer as the target indication. Further clinical studies in ovarian cancer are planned for the first quarter of 2008.

According to the agreement, Oasmia will receive payments of €4 million, partly up front and partly subject to a successful development and regulatory process for Paclical, as well as royalties from the sales.

Source: Oasmia

ImmunoCellular Therapeutics, Ltd. (IMUC) Agrees to Acquire Molecular Antibody Technology

ImmunoCellular Therapeutics, Ltd. (IMUC) has entered into a binding Memorandum of Agreement with Molecular Discoveries LLC (MDC), covering acquisition of all monoclonal antibody-related technology owned by MDC. The technology consists of a platform technology referred to by MDC as DIAAD(TM) for the potentially rapid discovery of monoclonal antibodies to detect and treat cancer and other chronic diseases and certain monoclonal antibody candidates for the potential detection and treatment of multiple myeloma, colon, small cell lung, pancreatic and ovarian cancers.

Under the terms of the acquisition, IMUC will issue 800,000 shares of IMUC's common stock to MDC. With the acquisition of this powerful technology, IMUC will have a full armamentarium of immune solutions for cancer: from cellular cancer vaccines that generate a long-lived response to an antibody-based therapy to kill cancer cells.

Source: IMUC