

Business & Regulatory Report

Approvals & Applications:

FDA Approves Novartis Agent Afinitor For Advanced Renal Cell Carcinoma

FDA has granted approval to Afinitor (everolimus tablets) for the treatment of advanced renal cell carcinoma after failure of treatment with sunitinib or sorafenib.

The agent is sponsored by Novartis Pharmaceuticals Corp.

The agent was approved on the basis of an international, multicenter, randomized, double-blind trial comparing everolimus to placebo. All patients received best supportive care. The trial was conducted in metastatic renal cell carcinoma after failure of treatment with sunitinib or sorafenib. Prior therapy with bevacizumab, interleukin-2, or interferon was also permitted.

Randomization was stratified according to prognostic score and prior

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Deals & Collaborations:

Roche Completes Purchase Of Genentech For \$46.8 Billion; R&D Stays In California

Roche (SWX: ROG.VX; R.O.S, OTCQX: RHHBY) Roche has completed its acquisition of **Genentech** (NYSE: DNA). The company sold \$95, pursuant to tender offer which expired March 25. Total acquisition price as \$46.8 billion.

The special committee of Genentech's Board of Directors has approved the agreement and recommends that Genentech shareholders tender their shares in Roche's tender offer.

Roche has owned a major stake in Genentech for over 18 years.

The combined company will be the seventh largest U.S. pharmaceuticals company in terms of market share. It will generate approximately \$17 billion in annual revenues and will employ around 17,500 employees in the U.S. pharmaceuticals business alone, including a combined sales force of approximately 3,000 people.

Research and early development will operate as an independent center within Roche from its existing campus in South San Francisco, retaining its talent and approach to discovering and progressing new molecules. Roche's Pharma commercial operations in the U.S. will be moved from Nutley, New Jersey to Genentech's site in South San Francisco.

The combined company's U.S. commercial operations in pharmaceuticals will operate under the Genentech name, leveraging the strong brand value of Genentech in the U.S. market. The existing U.S. sales organizations of

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FDA Approves Afinitor For Renal Cell Carcinoma

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anticancer therapy.

Altogether, 416 patients were randomized (2:1) to receive everolimus (n=277) or placebo (n=139). Progression-free survival (PFS) was the primary endpoint. The median PFS was 4.9 and 1.9 months in the everolimus and placebo arms, respectively (HR = 0.33, p value < 0.0001).

The treatment effect was similar across prognostic scores and prior treatment status. The overall survival results were not mature; 32% of patients had died by the time of data cut-off. The objective response rates were 2% and 0% for everolimus and placebo, respectively. After documented radiological progression, patients receiving placebo could receive everolimus.

The most common adverse reactions were stomatitis, infections, asthenia, fatigue, cough, and diarrhea. The most common grade 3/4 adverse reactions were infections, dyspnea, fatigue, stomatitis, dehydration, pneumonitis, abdominal pain, and asthenia. Anemia, hypercholesterolemia, hypertriglyceridemia, hyperglycemia, lymphopenia, and increased creatinine were the most common laboratory abnormalities.

The most common grade 3/4 laboratory abnormalities were lymphopenia, hyperglycemia, anemia, hypophosphatemia, and hypercholesterolemia. Deaths due to acute respiratory failure (0.7%), infection

(0.7%) and acute renal failure (0.4%) occurred on the everolimus arm but not on the placebo arm.

FDA has announced a collaboration with the Houston-based **Alliance for NanoHealth** and its eight member institutions to help speed development of safe and effective medical products in the emerging field of nanotechnology.

Under a Memorandum of Understanding, the FDA/ANH Nanotechnology Initiative will work to expand knowledge of how nanoparticles behave and affect biologic systems, and to facilitate the development of tests and processes that might mitigate the risks associated with nanoengineered products. All outcomes from this public-private partnership will be placed in the public domain for the benefit of all stakeholders.

The academic institutions include Baylor College of Medicine, M. D. Anderson Cancer Center, Rice University, the University of Houston, the University of Texas Health Science Center at Houston, Texas A & M Health Science Center, the University of Texas Medical Branch at Galveston, and the Methodist Hospital Research Institute.

“We are delighted with this partnership between the FDA and the eight institutions that constitute the Alliance for NanoHealth,” Larry Kaiser, president, the University of Texas Health Science Center, said in a statement. “We see this agreement as an important step on the path to taking advantage of the enormous power of nanotechnology to improve the diagnosis and treatment of disease.”

FDA’s collaboration with the ANH is administered through the agency’s Critical Path Initiative.

Arno Therapeutics Inc. (BULLETIN BOARD: ARNI) of Parsippany, N.J., said FDA accepted the company’s Investigational New Drug application for the use of AR-42.

AR-42 is an orally available, novel, potent, small molecule that modifies the acetylation of histones and other molecules, and is a targeted inhibitor of the Pan-DAC and Akt pathways.

HDAC inhibitors disrupt HDAC-PP1 complexes and cause signaling kinase dephosphorylation. In preclinical studies, AR-42 has demonstrated greater potency and a competitive profile in tumors when compared with vorinostat (also known as SAHA and marketed as Zolima by Merck), the leading marketed histone deacetylase inhibitor. Arno in-licensed the exclusive worldwide rights to AR-42 from The Ohio State University.



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GlaxoSmithKline (NYSE:GSK) said it has submitted two simultaneous regulatory applications to expand the use of Tyverb/Tykerb (lapatinib).

If approved, Tyverb/Tykerb could be used as a first-line therapy regimen combined with anti-hormonal therapy for patients with hormone-sensitive, metastatic breast cancer in Europe and the U.S.

The variation to the EU marketing authorization and the supplemental New Drug Application) were submitted respectively to the European Medicines Agency and to FDA for the combination of Tyverb/Tykerb plus an aromatase inhibitor based on the recent study, EGF30008. This study evaluated Tyverb/Tykerb in combination with letrozole in women whose breast cancer expressed was hormone receptor positive and may or may not also over-expressed the HER2+/ErbB2+ receptor.

These data were presented at the San Antonio Breast Cancer Symposium last December.

Therakos Inc. of Exton, Penn., said FDA has approved its CELLEX Photopheresis System for the palliative treatment of the skin manifestations of cutaneous T-cell lymphoma that are unresponsive to other forms of treatment.

The CELLEX Photopheresis System uses extracorporeal photopheresis, an innovative cellular therapy, to relieve the symptoms of CTCL. The system also has been cleared recently in Canada and Europe.

The new system features several improvements designed to enhance the patient treatment experience, such as shorter treatment times and reduced extracorporeal blood volume.

Specific features of the new system include an automated, closed system design that provides users the ability to switch between double and single needle treatment, if necessary. The system also utilizes a new, patented separation technology to separate white blood cells from whole blood.

Sopherion Therapeutics LLC, of Princeton, N.J., said it completed enrollment in its Phase III study of nonpegylated liposomal doxorubicin (Myocet) in metastatic HER-2-overexpressing breast cancer.

The study is a global, randomized, multicenter pivotal Phase III study in 363 patients who have metastatic HER-2-overexpressing breast cancer.

It will compare Sopherion's lead product in combination with the current standard of care, paclitaxel (Taxol) and trastuzumab (Herceptin(R)), vs. paclitaxel

and trastuzumab alone. Progression-free survival (PFS) is the primary efficacy endpoint, with monitoring for cardiac safety.

Eligibility criteria included no prior chemotherapy for metastatic disease, nor any trastuzumab, anthracyclines or taxanes within the previous 12 months. Eligible patients were randomized to receive either Myocet, paclitaxel and trastuzumab, or paclitaxel and trastuzumab alone in a 1:1 randomization ratio.

Myocet is a liposome-encapsulated doxorubicin-citrate complex. By encapsulating doxorubicin in a liposome—a manufactured, microscopic, vesicle consisting of discreet aqueous compartments surrounded by membranes composed of naturally occurring fats—its distribution in the body is altered in such a way as to reduce doxorubicin's toxicity, the company said.

OSI Pharmaceuticals Inc. (Nasdaq: OSIP) and Genentech Inc., (NYSE: DNA) said OSI submitted a supplemental New Drug Application to FDA for the use of Tarceva (erlotinib) as a first-line maintenance therapy for advanced non-small cell lung cancer patients who have not progressed following first-line treatment with platinum-based chemotherapy.

The companies announced that Roche, their international collaborator for Tarceva and owner of Genentech, filed an application in Europe with the European Medicines Agency.

“If approved, Tarceva will be the first EGFR targeted and oral therapy available as a first-line maintenance treatment for people with NSCLC, which we believe is an important advancement in the treatment of lung cancer,” Colin Goddard, OSI CEO said in a statement.

The submissions are based on a Phase III placebo-controlled, randomized, double-blind trial known as SATURN. In November 2008, OSI, Genentech and Roche announced that SATURN met its primary endpoint and showed that Tarceva significantly extended progression-free survival when given immediately following initial treatment with platinum-based chemotherapy, compared to placebo.

The SATURN study, conducted by Roche, enrolled 889 patients with advanced NSCLC at approximately 160 sites worldwide. Patients were treated with at least four cycles of standard first-line platinum-based chemotherapy and were then randomized to Tarceva or placebo if their cancer did not progress. The primary endpoint of the study was progression-free survival. Secondary endpoints included overall survival, safety and an evaluation of exploratory biomarkers.

Deals & Collaborations:

Roche Becomes 7th Largest U.S. Pharmaceuticals Firm

(Continued from page 1)

both companies will be maintained, resulting in a very strong presence in several specialty areas.

The transaction will provide the opportunity to simplify the structure of the combined organization and maximize the benefits of enhanced scale. Roche has already begun to wind down operations at its Palo Alto facility and will relocate the site's Virology research and development activities to South San Francisco.

Roche's Palo Alto Inflammation group is in the process of becoming part of Roche's Nutley research and development organization. Genentech's Late Stage Development and Manufacturing operations will be combined with the global operations of Roche, achieving substantial scale benefits, operational synergies and cost avoidance. Roche's manufacturing operations in Nutley will be closed and support functions, such as informatics and finance, will be consolidated with those of Genentech.

AMDL Inc. (NYSE Alternext US: ADL), of Tustin, Calif., said it has entered into a collaborative agreement with **Mayo Clinic** to conduct a clinical study for the validation of AMDL's next generation version of its US FDA-approved DR-70 (FDP) cancer test.

Through this validation study, AMDL and Mayo Clinic will perform clinical diagnostic testing to compare AMDL's DR-70 (FDP) cancer test with a newly developed, next generation test. The primary goal of the study is to determine whether AMDL's next generation DR-70 (FDP) test serves as a higher-performing test to its existing predicate test and can lead to improved accuracy in the detection of early-stage cancers.

For FDA regulatory approval on the new test, AMDL intends to perform an additional study to demonstrate the safety and effectiveness of the next generation test for monitoring colorectal cancer. The validation study will run for three months and final results are expected in the second or third quarter of 2009.

Micromet Inc. (NASDAQ: MITI), of Bethesda, Md., said that it is regaining from its partner **MedImmune** the rights in North America to its most advanced BiTE antibody candidate, blinatumomab, also known as MT103.

In Europe, Micromet is conducting a phase 2

clinical trial with blinatumomab for the treatment of patients with acute lymphoblastic leukemia and a Phase I clinical trial for the treatment of patients with non-Hodgkin's lymphoma.

The two companies plan to initiate a research program for the development of a new BiTE antibody for the treatment of hematological cancers. Micromet also announced its financial results for the fourth quarter and full year ended Dec. 31, 2008.

Samtheo Biopharma LLC of New York has entered into a license agreement, through its subsidiary, Lyndor Biosciences LLC, with **Moffitt Cancer Center**, gaining exclusive worldwide rights to a small molecule that selectively inhibits the activation of all three isoforms of Akt.

Persistent activation of the Akt pathway has been found to play an important role in oncogenesis and chemo- and radiation-resistance and to be responsible for cancer cell proliferation, survival and invasiveness.

Co-inventors are Jin Cheng, and Said Sebti, from Moffitt. "This small molecule is a highly selective and potent inhibitor of Akt activation, leading to tumor growth arrest and induction of cancer cell death, and results in overcoming chemoresistance," said Cheng, professor, Molecular Oncology Department at Moffitt.

"Patients whose tumors contain persistently activated Akt are predicted to be more likely to respond to this inhibitor either as a single agent or in combination therapy," said Sebti, professor and chair, Drug Discovery Department at Moffitt. "Akt is abnormally hyperactivated in many advanced malignancies and late stage tumors, such as breast, prostate, lung, pancreatic, liver, ovarian and colorectal cancers. Increased activation is also linked with drug and radiation resistance," said Cheng.

Through this license, Lyndor plans to develop and commercialize the new anti-cancer agent, which it refers to as LD-101, for refractory and resistant tumors as well as metastatic malignancies.

Clinical Trials:

Infinity Begins Phase II Trial Of Heat Shock Protein Inhibitor

Infinity Pharmaceuticals Inc. (NASDAQ: INFI), announced the initiation of a Phase II trial of IPI-504 (retaspimycin hydrochloride), a heat shock protein 90 (Hsp90) inhibitor, in combination with Herceptin (trastuzumab) in patients with human epidermal growth factor receptor 2 (HER2)-positive breast cancer.

"This trial will explore the combination of two

targeted agents, IPI-504 and trastuzumab (Herceptin), which should complement each other by disrupting HER2 signaling in different ways,” Clifford Hudis, chief of the Breast Cancer Medicine Service and Attending Physician at Memorial Sloan-Kettering Cancer Center and an investigator in the trial, said in a statement. “In earlier trials with a related agent we documented clear evidence of activity when Hsp90 inhibition is added to trastuzumab in patients with HER2-positive breast cancer.”

The goal of the open-label, international, multicenter Phase II trial is to evaluate the safety and anti-tumor activity of IPI-504 in combination with Herceptin in patients with pretreated, locally advanced or metastatic HER2-positive breast cancer, the company said. IPI-504 will be administered intravenously at 300 mg/m² on a three-week cycle, consisting of twice-weekly treatment for two weeks followed by one week off treatment. Herceptin will be administered intravenously once every three weeks. Evidence of anti-tumor activity will be evaluated using RECIST criteria (Response Evaluation Criteria in Solid Tumors).

The study will enroll 46 patients, and Infinity said it anticipates presenting preliminary data in mid-2010.

“By blocking HER2 signaling through a novel mechanism, IPI-504 may provide a new option for patients with HER2-positive breast cancer—one that may overcome resistance to HER2 targeted agents,” said Jose Baselga, chairman of the Medical Oncology Service and director of the Division of Medical Oncology, Hematology, and Radiation Oncology at the Vall d’Hebron University Hospital in Barcelona, Spain, professor of Medicine at the Universidad Autonoma de Barcelona and an investigator in the trial.

Preclinical data suggest that the HER2 oncoprotein is degraded rapidly when Hsp90 is inhibited by IPI-504, which eliminates HER2 signaling and ultimately causes the tumor cell to die. Infinity researchers have demonstrated that IPI-504 potently inhibits the growth of tumor cells when administered as a single agent in both Herceptin-sensitive as well as Herceptin-resistant breast cancer xenograft models, the company said. Moreover, in these models, the combination of IPI-504 and Herceptin results in more robust anti-tumor activity than when either agent was administered alone, the company said.

Infinity is evaluating Hsp90 inhibition in a range of cancers. These include The RING trial, an international Phase III registration trial in refractory gastrointestinal stromal tumors that positions IPI-504 as the potential first-in-class Hsp90 inhibitor. IPI-504 is also being

evaluated in a Phase II study in advanced non-small cell lung cancer and in a Phase Ib combination study with Taxotere (docetaxel) in patients with advanced solid tumors. Infinity is also evaluating its oral hsp90 inhibitor, IPI-493, in a Phase I study in patients with advanced solid tumors.

Celator Pharmaceuticals of Princeton, N.J., said that the first patient has been treated in its Phase II multicenter, randomized, open-label clinical trial of CPX-351 (Cytarabine:Daunorubicin) Liposome Injection versus intensive salvage therapy in adult patients (up to 60 years old) with acute myeloid leukemia in first relapse.

The study is supported through a partnership with The Leukemia & Lymphoma Society.

“CPX-351 represents a unique approach to enhancing the clinical benefit of the two most active drugs used in the treatment of patients with AML,” Jonathan Kolitz, director of the Leukemia Service at North Shore University Hospital and lead investigator for the study, said in a statement. “There is no standard of care established for patients in first relapse. We expect that this study will build on the promising results initially obtained in this patient population in the Phase I study and provide additional confirmation of the clinical benefit of CPX-351.”

The study (protocol CLTR0308-205) will enroll up to 120 patients between the ages of 18 and 60 who have pathological confirmation of relapsed AML after an initial complete response to prior therapy lasting at least one month. Patients will be randomized (2:1) to receive either CPX-351 (100u/m²; Days 1, 3, 5) or one of several control arm regimens, including high dose cytarabine with or without daunorubicin; conventional “7+3” (cytarabine/daunorubicin regimen); “MEC,” the mitoxantrone/etoposide/cytarabine regimen; and other published salvage regimens.

Patients will be monitored for all clinical adverse events as well as laboratory evaluations. The primary efficacy endpoint of the study is the comparison of overall survival at one year between the two arms. Secondary endpoints include complete remission rate and duration, event-free survival, aplasia rate, and rate of transfer for stem cell transplant. The study will be open for enrollment at leading institutions in the U. S. and Canada.

CPX-351 has been granted orphan drug status by FDA for the treatment of AML and is also currently being studied in a Phase II randomized trial comparing CPX-351 versus conventional cytarabine and daunorubicin

therapy (“7+3”) in patients 60-75 years of age with untreated AML, the company said.

Helix BioPharma Corp. (TSX, FSE: HBP) of Aurora, Ontario, said it has received the necessary regulatory approvals in Germany to initiate its planned Phase II pharmacokinetic study of Topical Interferon Alpha-2b in patients with low-grade cervical lesions.

The clinical study was designed, as mandated by regulatory authorities, to gather data on the absorption and elimination profile of Topical Interferon Alpha-2b in patients with low-grade cervical lesions, in addition to further data on its safety and efficacy. Depending on the data generated in the study, it is expected that interim results, which Helix anticipates will be received during its fiscal fourth quarter 2009, will allow the company to proceed with its planned regulatory filings in the U.S. and Europe respectively for its future Phase IIb and Phase III pivotal efficacy trials for this indication.

The primary objective of the clinical study is to determine the multiple-dose pharmacokinetic profile of Topical Interferon Alpha-2b following intravaginal application every other day of a total of 14 doses of the cream, the company said.

Following the pharmacokinetic portion of the trial, assessment of efficacy and safety parameters will continue until 35 doses of the cream have been applied. As such, the clinical study is designed to also provide support for the dosing regimen intended to be applied in the future to U.S. Phase IIb and European Phase III pivotal efficacy trials for this indication.

The study will be an open-label, single-arm trial in 28 female patients. Eligible women will be between 18 and 45 years of age and will present with a cytological diagnosis of Pap IIID, a colposcopic diagnosis of mild to moderate cervical dysplasia and confirmed human papilloma virus positive status.

The clinical study will be conducted under the direction of Achim Schneider, director of the Department of Gynecology at the Charite University Hospital in Berlin. The clinical portion of the study is expected to be completed during the first half of the 2010 calendar year.

Interferon alpha-2b is an immune system modulator that is active against a variety of HPV-induced lesions. Interferon alpha-2b is thought to function by triggering an antiviral response within infected cells, by activating certain intracellular enzymes which cause degradation of viral RNA, and by mobilizing the body’s natural immune system to destroy the infected cells. Interferon alpha-2b, which has been commercially available for

over 20 years, has been widely used by physicians as a treatment for certain HPV induced lesions, but is not generally favored due to the fact that conventional administration requires painful intradermal injection by a medical professional.

Nereus Pharmaceuticals Inc. of San Diego said it is conducting a randomized Phase II trial evaluating the vascular disrupting agent NPI-2358 in combination with Taxotere (docetaxel) in non-small cell lung cancer.

Preclinical and clinical data suggest that VDAs may be complementary or synergistic with chemotherapeutics and anti-angiogenesis agents due to the different targets and mechanisms of action, the company said. In addition, the non-overlapping side effect profile of VDAs compared to most other anti-cancer treatments makes them ideal candidates to employ in new combination therapies. Models combining NPI-2358 with docetaxel have produced particularly positive results in both efficacy and tolerability.

The ADVANCE (Assessment of Docetaxel and Vascular Disruption in Non-Small Cell Lung Cancer) trial will assess NPI-2358 in combination with docetaxel compared to docetaxel alone in patients with NSCLC who previously failed at least one chemotherapy regimen. Overall survival will be the primary endpoint of the trial, and progression free survival and tumor response rates will be compared as secondary endpoints. Approximately 150 patients will participate in the trial at sites in the U.S., Australia, India, and South America.

NPI-2358 is one of over 200 synthetic analogues that were prepared following the discovery of the compound Halimide isolated from a marine fungus, the company said. According to the company, the compound selectively attacks existing tumor blood vessels leading to hemorrhagic tumor necrosis without affecting normal vasculature, and it has a direct apoptotic effect on tumor cells.

Medivation Inc. (NASDAQ: MDVN) of San Francisco said it has received written permission from FDA to begin a pivotal phase III trial of MDV3100, its novel androgen receptor antagonist, in patients with metastatic castration-resistant prostate cancer who have failed docetaxel-based chemotherapy.

The placebo-controlled, double-blind, multinational trial will enroll approximately 1,200 patients who will be randomized (2:1) to receive either MDV3100 or placebo. The primary endpoint of the trial will be overall survival.

The FDA informed the company that it could

test a dose of MDV3100 up to 240mg/day. There are no driving or other restrictions placed on the activities of participants in the trial. Final trial specifics will be announced when the first patient is enrolled.

MDV3100 is being evaluated in an ongoing open-label, U.S., Phase I-II study of a total of 140 men with CRPC. Patients in this trial were heavily pretreated, with all having failed standard hormonal therapies and many having also failed docetaxel-based chemotherapy.

Micromet Inc. (NASDAQ: MITI) of Bethesda, Md., announced the commencement of a randomized, controlled Phase II trial of its human anti-EpCAM IgG1 antibody adecatumumab (MT201) for colorectal cancer after complete resection of liver metastases.

The trial has three arms comparing single agent adecatumumab to combination chemotherapy (FOLFOX: 5-FU/Leucovorin plus Oxaliplatin), and to FOLFOX followed by adecatumumab. The primary endpoint will be the disease-free survival rate at one year.

Apart from being the most highly and frequently expressed target antigen on colorectal cancer cells, EpCAM has recently been shown to drive tumor growth and to be expressed on colorectal cancer stem cells.

The ability of adecatumumab to potentially control and eliminate newly developing metastases has been suggested in a recently reported Phase II trial of adecatumumab as monotherapy in metastatic breast cancer, the company said. In that trial, patients with high levels of EpCAM expression, in a dose-dependent fashion, developed significantly less new lesions as compared to patients with low levels of EpCAM.

Rigel Pharmaceuticals Inc. (NASDAQ: RIGL) announced the enrollment of the first patient in a Phase II, multi-center clinical trial of R788 (fostamatinib disodium) in refractory or relapsed peripheral T-cell lymphoma.

The trial's primary objective is to assess the efficacy of R788, an orally bio-available Syk kinase inhibitor, in patients suffering from this subset of non-Hodgkin's lymphoma that originates in the patient's T-cells, the company said.

Prior studies have suggested increased expression of Syk at the cellular level in many of these patients with PTCL, the company said.

"Since we have seen that R788 shows clinical therapeutic benefit in certain types of B-cell lymphomas and that Syk kinase appears to play an important role in certain PTCLs, we believe that R788 may offer

new hope to the 12-15% of non-Hodgkin's lymphoma patients with the T-cell variety," Elliott Grossbard, executive vice president and chief medical officer of Rigel, said in a statement.

In general, patients with PTCL have a poorer prognosis and fewer treatment options than B-cell lymphoma patients.

The standard treatment regimen for PTCL—cyclophosphamide, hydroxydoxorubicin, vincristine (oncovin) and prednisone—fails provide adequate or durable responses in many patients.

The Phase II trial will be conducted in two stages at several centers in North America with each patient receiving 200mg of R788 twice a day for a minimum of 8 weeks, or until disease progression or withdrawal from the trial.

During stage one, 19 men and women with PTCL who have previously failed to respond to standard of care treatment for their disease are expected to be evaluated. Stage two is expected to include the enrollment of approximately 36 patients.

Efficacy will be assessed by CT/PET scans at baseline and CT scans of the disease-involved areas at 8 weeks. Safety will be assessed by periodic physical exams, blood tests and clinical laboratory work, among others. Results of the clinical trial are expected in the second half of 2010.

In June 2008, Rigel first reported results of a Phase II trial of R788 in the treatment of patients with relapsed or refractory B-cell non-Hodgkin's lymphomas.

R788 was well-tolerated in this patient population and showed therapeutic benefit in patients suffering from certain subcategories of the disease, especially small lymphocytic lymphoma/chronic lymphocytic leukemia and diffuse large B-cell lymphoma.

Tekmira Pharmaceuticals Corp. (TSX:TKM) announced that one of the company's collaborators, **Alnylam Pharmaceuticals, Inc.** (NASDAQ:ALNY), has initiated a Phase 1 human clinical trial of ALN-VSP in the United States. ALN-VSP, a product that utilizes Tekmira's SNALP technology, is being developed as a treatment for advanced liver cancers, including hepatocellular carcinoma and other solid tumors with liver involvement.

A milestone payment is payable to Tekmira upon the initiation of the Phase 1 trial and additional milestone payments become due as ALN-VSP is advanced through development.

Mark Murray, Tekmira's president and CEO, said, "We are pleased that Alnylam has initiated their

Phase 1 clinical trial of ALN-VSP as this represents an important milestone in the advancement of our SNALP technology. We will continue to support Alnylam and the ALN-VSP product as we manufacture the ALN-VSP clinical supplies on behalf of Alnylam.”

ALN-VSP contains small interfering RNA (siRNA) molecules formulated for systemic delivery with Tekmira’s SNALP technology. Tekmira has supported Alnylam in their advancement of ALN-VSP by generating preclinical data, providing analytical services and in the manufacture of ALN-VSP for clinical trials.

Pre-clinical data in mouse tumor model studies have demonstrated robust efficacy of ALN-VSP, including suppression of targeted genes, demonstration of an RNAi mechanism of action, tumor reduction, and extension of survival.

Alnylam’s ALN-VSP Phase I trial, being conducted in the U.S., is a multi-center, open label, dose escalation study designed to enroll approximately 55 patients with advanced solid tumors with liver involvement, who have failed to respond to or have progressed after standard treatment.

The primary objective is to evaluate the safety, tolerability, and pharmacokinetics of intravenous ALN-VSP, including demonstration of the maximum tolerated dose. Other exploratory objectives include the assessment of tumor response through Response Evaluation Criteria for Solid Tumors, a set of published guidelines that define when cancer patients’ disease improves, stabilizes or progresses during treatment; change in tumor blood flow or vascular permeability measured by DCE-MRI; and, change in plasma biomarkers of angiogenesis.

In addition, the analysis of pharmacodynamic effects of ALN-VSP on tumors will be measured in patients electing to proceed with voluntary pre- and post-treatment biopsies.

Oncology Management: **Pharma Invested \$65 Billion In Research & Development**

U.S. pharmaceutical research and biotechnology companies invested \$65.2 billion last year, an increase of roughly \$2 billion from 2007, the Pharmaceutical Research and Manufacturers of America and Burrill & Co. said.

This sets a new record, the association said.

Oncology accounts for the largest share of development activities. Altogether, there were 750

compounds in development for cancer, more than a quarter of the 2,900 agents in development in the U.S. Heart disease and stroke—with 312 compounds—is a distant No. 2, followed by 150 compounds for diabetes, 109 for HIV/AIDS and 91 for Alzheimer’s and dementia.

Poniard Pharmaceuticals Inc. (NASDAQ: PARD), of South San Francisco announced that it will concentrate its cash resources on the clinical and commercial development of its late-stage oncology candidate, picoplatin.

As a result, the company said it has discontinued its in-house preclinical research operations and reduced its workforce by approximately 12 percent, or eight employees, effective March 31. The company said it continues to evaluate strategic alternatives for its preclinical research programs.

“Concentrating our resources on advancing our lead product candidate, picoplatin, currently in Phase II and III clinical trials for the treatment of lung, colorectal and prostate cancers, supports our goal of commercializing picoplatin in 2010, initially for the treatment of small cell lung cancer,” Jerry McMahon, chairman and CEO, said in a statement.

US Oncology, Inc. has established US Oncology Clinical Development (USOCD), a full service contract research organization.

USOCD formalizes many of the services that US Oncology Research has provided since its inception in 1999. For more than a decade US Oncology Research has offered pharmaceutical and biotechnology companies elements of the clinical trial management process.

The formation of USOCD focuses the company’s extensive resources in order to provide full service CRO capabilities.

USOCD understands the complexities of oncology clinical trials and assists pharmaceutical and biotechnology companies in navigating the trial process to better manage their portfolio of products and expedite marketing approval. USOCD can identify key government and industry dynamics to intelligently plan and manage the enrollment strategy for clients.

“We have built an experienced team that enhances our ability to serve our clients for all of their oncology clinical trial needs,” said Steve Smith, vice president and general manager of Research and Personalized Science. “We will leverage all of the strengths of the US Oncology network and its proven history of accrual performance and commitment to quality.”