

# BIOWORLD® TODAY

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PAGE 1 OF 8

## Alkermes' Vivitrex Helps Men, Not Women, Reduce Drinking

**By Kim Coghill**  
**Washington Editor**

Preliminary results from a pivotal Phase III trial of Alkermes Inc.'s Vivitrex indicate that a once-monthly injection, along with psychosocial therapy, helps men reduce their rate of heavy drinking. However, the drug does not appear to work as well in women.

Alkermes, of Cambridge Mass., on Monday released favorable preliminary data from a six-month trial that enrolled 624 people described as heavy drinkers (five drinks a day for men and four for women). Trial participants were randomized to receive a combination of therapy plus once-monthly injections of 380 mg of drug, 190 mg of drug or placebo.

As it turns out, men in the 380-mg group demonstrated a 48 percent reduction in the rate of heavy drinking relative to placebo, a highly statistically significant outcome ( $p < 0.0001$ ),

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## Portola Series A Gets \$21M For Anti-Thrombotics Work

**By Randall Osborne**  
**National Editor**

With preclinical programs in cardiovascular research – certain parts of which were in-licensed from Millennium Pharmaceuticals Inc. – Portola Pharmaceuticals Inc. raised \$21 million in a Series A financing that will be used to advance the work.

"We've made hundreds of compounds around this chemistry scaffold, actually about a thousand now," said Charles Homcy, South San Francisco-based Portola's CEO and one of its founders. "We'll pick one of those in the first half of 2004, and then have it in man by the first half of 2005."

Privately held Portola plans to develop anti-platelet therapeutic agents for acute and chronic thrombotic indications, and is working on therapies for chronic inflammatory cardiovascular diseases such as atherosclerosis.

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### *American Society of Hematology Meeting*

## Various Phase III Studies Bolster Use Of Rituxan For Treating NHL

**By Aaron Lorenzo**  
**Staff Writer**

Drug development and marketing partners Genentech Inc. and Biogen IDEC Inc. touted a number of positive findings related to Rituxan at this week's American Society of Hematology meeting in San Diego.

The drug was shown to be effective as a first-line treatment of aggressive and indolent non-Hodgkin's lymphoma (NHL), the disease for which it is approved. Among the positive findings, the partners said one trial ended two years early – a Phase III randomized study that evaluated Rituxan (rituximab) in combination with chemotherapy as a front-line treatment for aggressive lymphoma, which met its primary efficacy endpoint early.

An interim analysis of data found a statistically signif-

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## NeoRx Placement Garner \$15.75M For STR Therapy

**By Randall Osborne**  
**National Editor**

Marching toward Phase III studies with its multiple myeloma treatment, NeoRx Corp. raised \$15.75 million in private placement of 1,575 newly created class of Series B convertible preferred stock to institutional investors.

The stock is convertible into about 3.15 million shares of common stock at \$5 per share, with no mandatory dividends payable.

NeoRx's shares (NASDAQ:NERX) closed Monday at \$5.02, up 14 cents.

Buyers of the convertibles also got five-year warrants to purchase an aggregate of 630,000 shares of common stock at \$6 per share, which could generate \$3.78 million more for the company.

The placement left NeoRx with about \$29 million in

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## CV Therapeutics Falls On FDA Briefing Document For Ranexa

By **Kim Coghill**  
Washington Editor

CV Therapeutics Inc.'s stock fell 27.2 percent a day in advance of its appearance before an FDA panel to present its new drug application for Ranexa (ranolazine), a chronic angina candidate.

The company's stock (NASDAQ:CVTX) Monday closed at \$12.21, down \$4.55. As is customary, trading will be suspended during the hearing of the Cardiovascular and Renal Drugs Advisory Committee Tuesday in Gaithersburg, Md.

In a series of letters and review papers comprising the FDA's "briefing document" for the candidate, government reviewers questioned certain safety issues, but seemed to believe that Ranexa could be approved under certain conditions.

The agency believes Ranexa produces an anti-angina effect as evidenced by improvement in exercise tolerance at peak in the two pivotal trials. Also supportive is a decrease in anginal attacks and nitroglycerin consumption. However, the agency said there have been no studies related to outcomes and it isn't known whether or not ranolazine affects survival.

A major safety issue, the FDA said, is repolarization. In addition, since ranolazine is metabolized via the cytochrome pathway, the potential arises for drug interactions leading to increased concentration, it said. Other issues include exploration of dosing and dose-response, establishment of benefit in women and benefit risk.

Finally, the FDA raised a concern over potential testicular toxicity in rats that manifested as impaired fertility.

CV Therapeutics, of Palo Alto, Calif., submitted its NDA last December and received an approvable letter from the agency in October. The panel hearing originally was scheduled for September, but postponed until December, a deci-

sion that did not impact the FDA's requirement to issue action by the end of October. (See *BioWorld Today*, Dec. 31, 2002; Aug. 5, 2003; and Nov. 3, 2003.) ■

## OTHER NEWS TO NOTE

• **Alexion Pharmaceuticals Inc.**, of Cheshire, Conn., reported that both the FDA and the European Agency for the Evaluation of Medicinal Products granted eculizumab orphan drug status for the treatment of PNH. Patients with PNH have a deficiency in certain protective proteins on the surface of their red blood cells, allowing their own complement system to attack and destroy those cells.

• **Angiogenix Inc.**, of Burlingame, Calif., started a Phase II trial of Acclaim in chronic angina. Acclaim (organic nitrate combined with L-arginine) is an oral product shown to induce coronary vasodilation while overcoming drug tolerance. The Phase II trial will enroll 170 patients with documented coronary artery disease who suffer from chronic, stable, effort-induced angina. The endpoint is treadmill walking time determined from the beginning of the exercise test until the patient develops angina of moderate degree.

• **Angiotech Pharmaceuticals Inc.**, of Vancouver, British Columbia, reported its intention to implement a 2-for-1 stock split, subject to shareholder approval. The company will seek approval at a special meeting of shareholders on Jan. 20. Angiotech is focused on enhancing the performance of medical devices and biomaterials through the use of pharmacotherapeutics.

• **Avigen Inc.**, of Alameda, Calif., exclusively licensed rights to the treatment of chronic pain using anti-inflammatory cytokines, including interleukin-10, from the University of Colorado. Avigen also expanded its existing sponsored research agreement with the University of Colorado at Boulder to further work in the treatment of chronic pain under way at the university's department of psychology and center for neuroscience.

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## Alkermes

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the company said. Women in the same group, however, showed no significant difference from placebo.

"This result is particularly striking when one considers that this difference is a 48 percent reduction from a placebo group whose drinking activity is also declining during the study due to the positive impact of psychosocial counseling and, possibly, the psychological impact of the placebo injection," Elliot Ehrich, Alkermes' chief medical officer, said during a conference call Monday.

The results then beg the question, why didn't females respond as well?

"Based on our analysis in prior studies, we had prepared for different responses to gender," Ehrich said. "However, we were surprised at the extent of the difference. We have a lot more work to do here in order to understand the results and we would expect to identify and pursue clinically various hypotheses in the future."

Two-thirds of patients in the study were male, which is representative of the alcohol-dependent population, the company said.

In the overall study population, patients treated with 380 mg of drug experienced about a 25 percent reduction in the rate of heavy drinking relative to placebo, a statistically significant number ( $p=0.03$ ). And in the overall 190-mg group, patients in the treatment arm experienced a 17 percent reduction in the rate of heavy drinking relative to placebo with a trend toward statistical significance ( $p<0.10$ ).

Men in the treatment arm of the 190-mg group demonstrated a 25 percent reduction in the rate of heavy drinking, also statistically significant ( $p<0.03$ ).

While the overall study population produced statistically significant results, Ehrich cautioned that it would be incorrect to infer that reduction is representative of the treatment effect across all patients when, in fact, the entire effect was observed in the male population.

Vivitrex is a long-acting formulation of naltrexone based on Alkermes' Medisorb injectable extended-release technology. Using the technology, naltrexone is encapsulated in microspheres made of a biodegradable polymer that dissolves slowly and releases drug at a controlled rate following intramuscular injection.

Richard Pops, Alkermes' CEO, told *BioWorld Today* complete results of the Phase III will be submitted for publication in a peer-reviewed journal. He declined to speculate on a timeline for publication.

However, he did say the company hopes to file for regulatory approval in the U.S. in the first half of 2005. The application will be based on the single Phase III.

Despite a great level of interest in Vivitrex, Pops said, the company hasn't decided whether to partner the product in the U.S. The company likely will seek a partner for markets abroad, though.

In the weeks prior to learning of Vivitrex's potential,

the FDA approved Risperdal Consta (risperidone, long-acting injection) for schizophrenia. Alkermes' partner, Janssen Pharmaceutica Products LP, a unit of Johnson & Johnson, of New Brunswick, N.J., launched the product last week. (See *BioWorld Today*, Oct. 31, 2003.)

As for the success of both Risperdal Consta and Vivitrex, Pops said the company has accomplished two of its major milestones for 2003. "In terms of fundamentals of the company, as we go forward into 2004, we feel we are on strong footing," he said.

Alkermes' stock (NASDAQ:ALKS) closed Monday at \$12.78, down 25 cents. ■

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## Portola

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The Jan. 11, 2001, issue of *Nature* reported the cloning of a previously unidentified ADP receptor, an important mediator of platelet activation that is the target of two existing anti-clot drugs, ticlopidine and clopidogrel.

Portola's "idea here is to have a one-a-day oral drug, but it will also be available as [intravenous administration]," Homcy said. "This would be for prevention of death, myocardial infarction, stroke, re-hospitalization for ischemia and [problems related to] peripheral vascular disease – all of the thrombotic complications that occur in patients with atherosclerosis."

Homcy and others who founded Portola have backgrounds with Cambridge, Mass.-based Millennium. Homcy most recently served as the company's president of research and development and before that was vice president of research and development for COR Therapeutics Inc., also of South San Francisco, with which Millennium merged in a stock transaction worth about \$2 billion. (See *BioWorld Today*, Dec. 7, 2001.)

"This technology actually started at COR," Homcy told *BioWorld Today*. Millennium "for a variety of reasons" chose not to pursue it, so now "the same people who were working on it at COR for many years are the people who will continue to work on it."

Robert Scarborough, another co-founder of Portola, was formerly vice president of cardiovascular chemistry at Millennium and before that served as vice president of medicinal chemistry of COR. Scarborough is credited with inventing the firm's cardiovascular drugs Integrilin (eptifibatide) – gained in the COR merger – and Natrecor (nesiritide).

Portola co-founder David Phillips also helped establish COR, and most recently was the principal research scientist at Millennium. Scarborough and Phillips are senior vice presidents of Portola, which began operating this year and has 32 employees, including 11 chemists and nine biologists.

The financing round was co-led by Sutter Hill Ventures, of Palo Alto, Calif.; Prospect Ventures, also of Palo Alto; and MPM Capital, of Boston. Making what the company described as "significant" investments were Abingworth Management, of London, and Frazier Healthcare Ventures, of Seattle. ■

## Meeting

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icant improvement in time to treatment failure for patients receiving Rituxan and chemotherapy, compared to chemotherapy alone. The study was conducted worldwide.

Dubbed the MabThera International Trial, the study enrolled about 800 patients in 18 countries and was sponsored by F. Hoffmann-La Roche Ltd. Rituxan is labeled MabThera outside the U.S., where it is marketed by Basel, Switzerland-based Roche. In the U.S. it is held jointly by Biogen IDEC and Genentech, which also reported plans to repurchase up to \$1 billion of its common stock through Dec. 31. Rituxan is co-marketed in Japan by Roche and Zenyaku Kogyo Co. Ltd., of Tokyo.

Separately, initial results from another Phase III randomized study showed that NHL patients who received Rituxan plus cyclophosphamide, doxorubicin, vincristine and prednisone (CHOP) chemotherapy, followed by Rituxan maintenance therapy or observation, demonstrated a trend toward prolongation of time to treatment failure, the primary endpoint of the induction phase of the study, as compared to patients who received CHOP alone followed by Rituxan maintenance or observation. The addition of Rituxan to CHOP did not influence the overall response rate in the induction phase (78 percent for R-CHOP vs. 77 percent for CHOP alone).

With regard to the primary endpoint for the maintenance phase of the study, patients treated with Rituxan maintenance for up to an additional two years after completing induction therapy had a statistically significant prolongation in time to treatment failure, compared to patients who did not receive Rituxan maintenance therapy following induction. The advantage appeared predominantly confined to patients who received CHOP alone during the induction phase. Also, investigators found no difference in overall survival between the Rituxan maintenance and observation arms, though they said additional follow-up is necessary.

The E4494 trial was a U.S. Intergroup study led by the Eastern Cooperative Oncology Group, in collaboration with the Southwest Oncology Group and the Cancer and Leukemia Group B.

Initial Phase III results in patients with indolent NHL demonstrated that the addition of Rituxan to cyclophosphamide, vincristine and prednisone chemotherapy (R-CVP) prolonged time to treatment failure – the study's primary endpoint – to 26 months, compared to seven months for patients treated with CVP alone. The risk of an event (defined as disease progression, relapse, death, stable disease after cycle four or new treatment administered) was reduced by 66 percent in patients who received R-CVP.

Phase II results in indolent NHL patients showed that those who received Rituxan maintenance therapy experienced 31 months of progression-free survival as compared

to eight months for those who were retreated with Rituxan at the time of disease progression. The study also demonstrated that duration of Rituxan benefit, the study's primary endpoint, can be prolonged by either maintenance therapy (31 months) or re-treatment (27 months).

In other news from the meeting:

- **Amgen Inc.**, of Thousand Oaks, Calif., said interim data showed that after 12 weeks of treatment with Aranesp (darbepoetin alfa), administered every two weeks in correcting anemia in cancer patients not undergoing chemotherapy, the mean change in hemoglobin was 1.9 g/dL for the Aranesp group and 0.2 g/dL in the control group. The randomized, multicenter study also found that the Kaplan-Meier estimate (95 percent) of hematopoietic response was 81 percent for the Aranesp group and 26 percent for the control group. Findings from separate head-to-head studies showed that 200 mcg of Aranesp dosed once every two weeks provided similar results to 40,000 units of epoetin alfa dosed once weekly in boosting hemoglobin and reducing the need for blood transfusions in cancer patients undergoing chemotherapy.

- **AnorMED Inc.**, of Vancouver, British Columbia, said treatment with AMD3100, its lead drug candidate for stem cell transplantation, helped poor mobilizers generate an adequate number of stem cells required for a transplant procedure. More specifically, Phase II results showed that when AMD3100 was used in combination with a standard agent called G-CSF, all 19 patients achieved the target number of stem cells for transplantation. But seven of the 19 did not reach the target number when G-CSF was used alone to collect their cells.

- **BioCryst Pharmaceuticals Inc.**, of Birmingham, Ala., reported Phase I results showing that treatment with intravenous BCX-1777 resulted in a clinical effect in four of five patients with aggressive T-cell malignancies, as evidenced by a decrease in malignant cell counts. The drug was well tolerated, with few drug-related adverse events. The company added that it expects data from several additional ongoing trials of the product in the first half of next year. Its stock (NASDAQ:BCRX) dropped 86 cents Monday, or 10.2 percent, to close at \$7.54.

- **Biogen IDEC Inc.**, of Cambridge, Mass., said new data support the ability of Zevalin (ibritumomab tiuxetan) to induce long-term remissions in patients with relapsed, refractory or transformed indolent B-cell NHL. Also, preliminary results indicate that Zevalin has promising clinical activity in treating patients with mantle-cell lymphoma.

- **Cell Genesys Inc.**, of Foster City, Calif., said interim Phase II data indicate that its GVAX cancer vaccine is well tolerated and might reduce residual leukemic cells that persist after chemotherapy, as indicated by decreased levels of WT-1, a leukemia-associated genetic marker, which is detectable in more than 95 percent of patients with active

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## Meeting

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acute myelogenous leukemia. Patients with newly diagnosed leukemia were treated with chemotherapy, and, if responsive, subsequently received autologous bone marrow stem cell transplantation and GVAX.

• **Cell Therapeutics Inc.**, of Seattle, said preliminary clinical data showed that following treatment with Trisenox (arsenic trioxide), in 28 of 120 myelodysplasia patients with sufficient data for evaluation, responses were observed in each of the cell lineages and were seen after about eight to 24 weeks of therapy. Also, Trisenox treatment led to transfusion independence in 12 patients and a decrease of 50 percent or more in transfusion requirements for an additional five patients. Responses to Trisenox lasted from just under eight weeks up to 46 weeks, with a median duration of about 15 weeks. Separately, the company said data from preclinical studies show that a new cancer target called LPAAT-beta is highly expressed in many cancers.

• **Corixa Corp.**, of Seattle, and **GlaxoSmithKline plc**, of London, said results from several studies showed that Bexxar (tositumomab and iodine I-131 tositumomab) is active in a variety of patients with difficult-to-treat lymphomas, including patients with heavily pre-treated follicular NHL who have had multiple relapses, patients who initially responded but subsequently relapsed following the Bexxar therapeutic regimen, and patients with previously untreated mantle-cell lymphoma who received Bexxar as a component of sequential therapy. The product is approved for use in a single course for treating patients with CD20+, follicular NHL, with and without transformation, whose disease is refractory to the antibody treatment rituximab and has relapsed following chemotherapy.

• **Cytogen Corp.**, of Princeton, N.J., said clinical data showed that Quadramet (samarium SM 153 leixidronam injection), in combination with zoledronic acid (Zometa, Novartis AG), provided pain relief in elderly patients with symptomatic chemotherapy-refractory multiple myeloma. Findings from another study suggested a benefit in using high-dose Quadramet in multiple myeloma patients, along with high-dose melphalan chemotherapy (200 mg/m<sup>2</sup>), prior to undergoing stem cell transplantation.

• **EntreMed Inc.**, of Rockville, Md., said preliminary Phase II data demonstrated that Panzem is well tolerated and stabilized disease in patients with plateau or relapsed multiple myeloma. The company plans to continue evaluating the patients using a new formulation of the drug candidate, designed to increase and prolong exposure to Panzem. Separately, EntreMed said it developed compounds that specifically inhibit proteinase-activated receptor-2 (PAR-2), which is associated with inflammation and has been shown in preclinical models to play a critical role

in tumor growth and formation of new blood vessels. The company said in vivo studies showed that a small-molecule peptidomimetic is more potent in blocking the signaling of PAR-2 than a peptide it also designed.

• **Genitope Corp.**, of Redwood City, Calif., said Phase II results suggest that an accelerated schedule with more doses of MyVax Personalized Immunotherapy might be a safe and effective treatment following chemotherapy in individuals with aggressive lymphoma, including mantle-cell lymphoma. The median time to disease progression for mantle-cell patients who received five immunizations during 24 weeks was 254 days following completion of chemotherapy. In such patients who received eight doses over 18 weeks, the median time to disease progression was 477 days following completion of chemotherapy.

• **Genmab A/S**, of Copenhagen, Denmark, reported interim Phase II results showing that treatment with HuMax-CD4 in cutaneous T-cell lymphoma patients resulted in at least a partial response (more than 50 percent improvement) among 55 percent of early stage and 38 percent of advanced-stage patients. One early stage patient's disease was completely cleared, and 9 percent of early stage and 23 percent of advanced-stage patients achieved a minor response (25 percent to 50 percent improvement). Separately, Genmab reported preclinical findings showing that HuMax-CD20 binds to a unique site on CD20 target cells when compared to other known CD20 antibodies. Other data showed that HuMax-CD20 appears to stop growth of B-cell tumors grown from a laboratory cell line more effectively than placebo or Rituxan.

• **Genta Inc.**, of Berkeley Heights, N.J., said results from several clinical studies pointed to the safety and, potentially enhanced activity, when chemotherapy was combined with its lead cancer drug, Genasense (oblimersen sodium), as initial therapy for acute myeloid leukemia patients older than 60. Other clinical results suggested that Genasense could be used to synergistically enhance the activity of Rituxan in NHL.

• **Geron Corp.**, of Menlo Park, Calif., said preliminary Phase I/II results showed that treatment with its telomerase therapeutic vaccine for metastatic prostate cancer has resulted in telomerase-specific cellular immune responses among all but one of the patients evaluated to date. No patients exhibited any sign of treatment-related adverse effects, and in the three patients analyzed thus far from the high-dose group, stabilization of serum PSA values during the treatment phase was observed.

• **Hollis-Eden Pharmaceuticals Inc.**, of San Diego, reported positive results with investigational immune-regulating hormones (IRHs) in models of radiation and chemotherapy-induced neutropenia. The findings included a second study in nonhuman primates showing beneficial effects with HE2100 (Neumune) in a model of radiation

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injury, as well as positive results from separate studies in nonhuman primates with both Neumune and a new IRH in carboplatin-induced neutropenia. Other data related to Neumune's mechanism of action showed that the compound acts directly on a number of important stem cell components.

- **Immunomedics Inc.**, of Morris Plains, N.J., said unlabeled epratuzumab could be combined safely with rituximab and the CHOP chemotherapy regimen in patients with aggressive NHL. The study also showed that epratuzumab could be active when given as re-treatment after an earlier response in patients with indolent NHL who relapsed after chemotherapy. Other data showed that the pharmacokinetic behavior of rituximab and epratuzumab were not altered when the antibodies were given in a combination therapy. Its stock (NASDAQ:IMMU) dropped 81 cents Monday, or 15.1 percent, to close at \$4.54.

- **ILEX Oncology Inc.**, of San Antonio, said investigator-sponsored studies showed that Campath (alemtuzumab) cleared residual bone marrow disease in most patients following chemotherapy and a molecular remission was achieved in 11 of 29 patients in whom polymerase chain reaction results were available. The overall response rate was 53 percent. Researchers reported that the absence of minimal residual disease is the best predictor for prolonged survival of patients with chronic lymphocytic leukemia. Campath is approved for treating B-cell chronic lymphocytic leukemia. Separately, ILEX said adults with first relapsed and primary refractory acute myeloid leukemia or myelodysplastic syndrome who were treated with the combination of clofarabine and ara-C (cytarabine) achieved an overall response rate of 41 percent in a Phase I/II trial. The response rate from the Phase II study included seven complete remissions and five complete remissions without platelet recovery. Six weeks ago, ILEX submitted the first part of a new drug application for use of clofarabine for refractory or relapsed pediatric acute leukemia. The company obtained U.S. and Canadian development rights from **Bioenvision Inc.**, of New York, which maintains rights outside those areas. (See *BioWorld Today*, Oct. 23, 2003.)

- **Inex Pharmaceuticals Corp.**, of Vancouver, British Columbia, released results from three separate clinical trials indicating that its lead anticancer product, Onco TCS, is able to reduce the size of tumors in lymphoma patients with advanced disease. Among the findings, final pivotal data on 119 patients with relapsed aggressive NHL resulted in a 25 percent overall response rate after Onco TCS treatment. The findings included eight patients whose tumors were completely eliminated and 22 whose tumor volume was reduced by more than 50 percent. An additional 31 patients had their disease stabilized while being treated. Initial results of the study were reported during the sum-

mer, and the company began a rolling new drug application with an initial submission to the FDA two months ago. (See *BioWorld Today*, Oct. 1, 2003.)

- **Novartis AG**, of Basel, Switzerland, said new data demonstrated that at 12 months, newly diagnosed patients with Philadelphia chromosome positive chronic myeloid leukemia taking 800 mg/day of Gleevec (imatinib mesylate) achieved higher complete cytogenetic responses compared to those taking the standard 400-mg/day dose. More specifically, 92 percent of evaluable patients taking 800 mg achieved a response, compared to 72 percent on the standard dose. More patients in the higher dose group also achieved a molecular response compared to those in the standard dose group.

- **Seattle Genetics Inc.**, of Bothell, Wash., said Phase I data showed that its SGN-30 product was well tolerated and demonstrated antitumor activity. Also, preclinical data on SGN-40 showed activity in multiple models of hematologic malignancies and favorable pharmacokinetic properties. The company added that it expects to begin Phase II trials early next year to evaluate SGN-30 in patients with Hodgkin's disease or anaplastic large-cell lymphoma, and to begin a Phase I study of SGN-40 in multiple myeloma patients.

- **SuperGen Inc.**, of Dublin, Calif., said data from five clinical studies demonstrated the activity of its cancer drug Nipent (pentostatin for injection), as part of combination therapy, in chronic lymphocytic leukemia. The company added that findings from two other clinical studies demonstrated the drug's activity in treating NHL patients through combination therapy. Nipent is approved as a single-agent treatment for patients with hairy-cell leukemia.

- **Trubion Pharmaceuticals Inc.**, of Seattle, said its initial products demonstrated effectiveness in depleting normal and malignant B cells. Data from one study demonstrated that its TRU-016 small modular immunopharmaceutical (SMIP) binds to and effectively kills malignant B cells through apoptosis, complement-dependent cytotoxicity and antibody-dependent cellular cytotoxicity. In a second study, injection of another SMIP labeled TRU-015 into macaques resulted in rapid and complete depletion of circulating B cells for more than 28 days following the second injection.

- **VasGene Therapeutics Inc.**, of Los Angeles, reported clinical data showing that its Veglin product can be administered safely in a number of cancers and HIV-related malignancies through eight escalating dose levels. The company called the product a next-generation inhibitor of vascular endothelial growth factor (VEGF), which employs a three-prong approach to inhibiting tumor growth. There was no evidence of hypertension or other side effects seen with other VEGF antagonists. Used as a single agent, Veglin also demonstrated evidence of tumor response following one or two cycles of therapy in some patients. ■

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## OTHER NEWS TO NOTE

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- **Benitec Ltd.**, of Queensland, Australia; Commonwealth Scientific and Industrial Research Organisation (CSIRO) in Canberra, Australia; and the Queensland Department of Primary Industries in Queensland, entered a strategic agreement that will accelerate Australia's lead in the global commercialization of DNA Directed RNA interference, a gene silencing technology. Called ddRNAi, the technology was invented in Australia and is designed to be used in bioresearch institutes, biotech and pharmaceutical companies worldwide. Benitec will focus on commercializing ddRNAi for human applications including research models used in functional proteomics. CSIRO will focus on nonhuman applications, including plants, animals and insects. Queensland DPI will continue its ddRNAi research and will have access to both Benitec and CSIRO's global commercialization pathways.

- **Biomira Inc.**, of Edmonton, Alberta, and **Merck KGaA**, of Darmstadt, Germany, reported a final analysis of Phase III data at the San Antonio Breast Cancer Symposium related to their study of the Theratope vaccine in women with metastatic breast cancer. Early this summer, the partners said the study failed to meet two pre-determined statistical endpoints – time to disease progression and overall survival – though analysis of Theratope-treated patients in one pre-stratified subset of more than 300 women who received hormonal treatment following chemotherapy and appeared to show a favorable trend toward improvement in survival. The added analyses revealed a median time to disease progression of 8.3 months for patients treated with Theratope vs. 5.8 months for those on control (Cox  $p=0.220$ ; Log Rank  $p=0.207$ ). The median survival was 38.2 months in the Theratope arm vs. 30.7 months in the control arm (Cox  $p=0.077$ ; Log Rank  $p=0.066$ ). (See *BioWorld Today*, June 18, 2003.)

- **BioSante Pharmaceuticals Inc.**, of Lincolnshire, Ill., reported preclinical data at last week's Pharmaceutical Education Associates symposium on Inhalation Drug Delivery in Princeton, N.J., showing that its BioAir calcium phosphate nanoparticulate delivery system for inhalable insulin significantly increased the systemic residence time and duration of action of the insulin. More specifically, the amount of insulin that became available through the bloodstream was 1.8 times more than that of injected insulin.

- **Cel-Sci Corp.**, of Vienna, Va., reported the publication of data from a Phase I/II trial in 54 advanced primary head and neck cancer patients. The data demonstrated that treatment with Cel-Sci's immunotherapy drug Multikine rendered the majority of cancer cells susceptible to radiation therapy. The increased sensitivity of the Multikine-treated tumors to radiation was derived from an increase in the number of proliferating cancer cells. Following treat-

ment, the majority of the tumor cells were in a proliferative state. Control patients had lower expression of the same proliferation marker, Ki67, in the study ( $p<0.05$ ). The data were published in the December 2003 issue of *The Laryngoscope*.

- **Crucell NV**, of Leiden, the Netherlands, signed a service agreement with **Progenics Pharmaceuticals Inc.**, of Tarrytown, N.Y., whereby Crucell will undertake the development of a cell line based on its PER.C6 technology for the production of a recombinant protein product candidate for Progenics. Crucell will receive payments on reaching milestones outlined in the program. Further financial details were not disclosed. Crucell's PER.C6 technology is designed to offer a safe and scalable cell line for the production of a range of biologics.

- **Gen-Probe Inc.**, of San Diego, and **Tosoh Corp.**, of Tokyo, cross-licensed intellectual property covering certain nucleic acid-testing technologies. The licenses, which are effective Jan. 1, cover products in clinical diagnostics and other related fields. Tosoh will receive nonexclusive rights to Gen-Probe's transcription-mediated amplification and ribosomal RNA technologies in exchange for two payments totaling \$7 million in 2004. Additionally, Tosoh will pay Gen-Probe royalties on worldwide sales of products that employ the licensed Gen-Probe technologies.

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### NeoRx

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cash and investment securities, enough to fund operations into 2005, and the company said its first patients are expected to enroll into the Phase III trial during 2004's first quarter.

NeoRx officials could not be reached for comment.

STR delivers high doses of radiation to tumor sites in the skeleton with minimal damage to organs outside the bone, NeoRx said, targeting bone and adjacent marrow with a small-molecule agent known as DOTMP, combined with the radionuclide holmium-166.

NeoRx plans to conduct a randomized, controlled study of STR in patients with the primary refractory form of bone marrow cancer, enrolling about 240 evaluable subjects, half in the experimental arm and half as controls.

Patients in the experimental arm will get STR plus the chemotherapy drug melphalan, followed by autologous stem cell transplantation, and the control patients will get melphalan only, followed by transplantation.

In the spring, the FDA lifted its clinical hold on NeoRx's Skeletal Targeted Radiotherapy program, and in October the company said it had reached an agreement with the agency for a Phase III trial protocol. The company said then it was seeking a partner to help with Phase III costs and marketing. (See *BioWorld Today*, April 25, 2003, and Oct. 2, 2003.)

Serving as placement agent in the deal was Leerink Swann & Co. in Boston. ■

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## OTHER NEWS TO NOTE

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• **Immtech International Inc.**, of Vernon Hills, Ill., said its oral drug candidate, DB289, demonstrated anti-malarial activity in a clinical trial conducted in Bangkok, Thailand. The results were presented at the annual meeting of the American Society of Tropical Medicine and Hygiene on Dec. 6 in Philadelphia. Of 32 treated patients, nine were infected with *Plasmodium vivax* and 23 patients with *Plasmodium falciparum*, the most deadly form of malaria found in humans. All the patients cleared the malaria parasite and malaria symptoms. Fifty percent of the patients cleared the parasite within 24 hours of the first dose. Of the 23 patients treated for *P. falciparum*, the cure rate was 91 percent as two of the patients had malaria in the 28-day after-treatment period, but it could be the result of re-infection, the company said.

• **Kosan Biosciences Inc.**, of Hayward, Calif., started a Phase II trial within its partnership with **F. Hoffmann-La Roche Ltd.**, of Basel, Switzerland, to evaluate the efficacy of KOS-862 as a monotherapy for colorectal, non-small-cell lung and metastatic breast cancers. KOS-862 is one of Kosan's two lead oncology programs and is a polyketide that inhibits cancer cells by the same mechanism as paclitaxel. In preclinical models, it was shown to be effective against paclitaxel-resistant tumors.

• **Microscience Ltd.**, of London, entered a Cooperative Research and Development Agreement with the Naval Medical Research Centre in Silver Springs, Md. The collaboration will evaluate preclinically what Microscience believes will be the first oral anthrax vaccine to enter human testing. Under the CRADA, Microscience will provide its spi-VEC delivery system, which has been engineered to deliver anthrax antigens, either as protein or DNA, via an oral route.

• **Noven Pharmaceuticals Inc.**, of Miami, said the FDA issued recommendations regarding the company's proposed study design for MethyPatch, a development methylphenidate transdermal system for attention deficit hyperactivity disorder. The FDA also accepted for filing the abbreviated new drug application for Noven's developmental transdermal fentanyl system for chronic pain. The company said it is working with partner **Shire Pharmaceuticals Group plc**, of Andover, UK, to review and respond to the FDA's comments regarding study design.

• **Proneuron Biotechnologies Inc.**, of Los Angeles, said that enrollment in its Phase II trial of ProCord now is open to patients at Craig Hospital in Denver. Proneuron focuses on the development of treatments for patients with spinal cord injuries and other acute and chronic disorders of the central nervous system. ProCord consists of autologous activated macrophage therapy for a randomized trial for patients with acute complete spinal cord injury within

14 days of injury.

• **Quigley Corp.**, of Doylestown, Pa., said an independent in vitro study conducted by **Retroscreen Virology Ltd.** (an affiliate of the University of London) demonstrated that Quigley test compounds previously tested on the influenza virus showed "significant virucidal activity against the Urbani strain of the severe acute respiratory syndrome virus." The compound was demonstrated to be 100 percent effective in preventing influenza A in ferrets in an earlier study.

• **Scynexis Europe Ltd.**, of Cambridge, UK, and **GeneCare Research Institute Co. Ltd.**, of Kamakura, Japan, reported details of a new deal between the companies. Scynexis will provide a range of drug discovery, synthesis and purification services to support GeneCare Research Institute's ongoing work in the field of anti-inflammatory drugs. Using Scynexis' HEOS operating system, hit explosion work will be undertaken to develop compound libraries for subsequent screening by GeneCare Research Institute. HEOS also will be used for lead optimization to identify clinical candidates. Terms of the deal were not disclosed.

• **Tripos Inc.**, of St. Louis, and **Biovitrum AB**, of Stockholm, Sweden, released favorable results from the companies' discovery research partnership. In less than three months, Tripos successfully designed and synthesized a lead series for one of Biovitrum's high-priority projects. The partners also entered a new collaborative software research program to develop improved tools for drug discovery. Biovitrum's acquisition of new LeadQuest compounds to augment its existing screening library coupled with Tripos' software programs (ChemSpace and SARNavigator) allowed the companies to identify and optimize two lead series for follow-up.

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