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PAGE 1 OF 7

EPO Warning Nicks Amgen; Off-Label Risks Told Earlier

By Aaron Lorenzo and Randall Osborne
Staff Writers

Amgen Inc. headed off worse damage from Friday's news of the "black box" label warning for the firm's flagship red-blood cell boosters Aranesp and Epogen by pointing out that problems arise mainly in cases where the drugs are given at levels beyond those approved, and such cases rarely occur.

Richard Pazdur, director of the FDA's Office of Oncology Drug Products, called for "discretion on the part of the treating physician." They are exercising it, at least according to data gathered by researchers of cancer physicians, published separately Friday.

The label change itself, accepted by the FDA, could make life easier for the company May 10, when Amgen will take part in the agency's Oncologic Drugs Advisory Com-
See Amgen, Page 4

Neose Raising \$43.3M Through A Placement Of Stock, Warrants

By Jim Shrine
Staff Writer

Neose Technologies Inc., which was running a little low on cash, is raising about \$43.3 million through a private placement to fund development of its pegylated protein programs.

However, the Horsham, Pa.-based firm is selling nearly 40 percent of the company in the deal, a total that would increase to about 48.6 percent if all warrants attached to the sale were exercised.

The deal, expected to close Tuesday, entails the sale of about 21.44 million shares and warrants to purchase about 9.65 million shares, at \$2.02 per unit. The unit price was based on the \$1.96 closing price Thursday, plus 12.5 cents per full warrant (which added nearly 6 cents per unit).

The five-year warrants are exercisable at \$1.96 per
See Neose, Page 5

Location, Location, Location: Ceregene Bets on Better Delivery

By Cynthia Robbins-Roth
BioWorld Today Columnist

As I head into my mid-50s, I have daily reminders that neurodegenerative diseases are huge problems. In addition to my own memory lapses, my family and my friends' families are affected by head trauma, Alzheimer's, ALS, multiple sclerosis and Parkinson's. Millions around the world lose the ability to function in society from those ailments.

It's only been in the past two decades that we've had any hints about the molecular underpinnings of neurodegeneration. A grab bag of relevant genetic mutations and cell interactions have been identified, but we still really don't know what is causing the gradual loss of nerve function or how to stop it.

Back in the late 1980s and 1990s, when protein replacement was biotech's primary strategy, Amgen, Chiron, Regeneron, Cephalon and others embarked on quests to
See Ceregene, Page 6

Eyeing Public Markets, Jazz Files For IPO To Raise \$172M

By Jennifer Boggs
Staff Writer

Specialty pharma firm Jazz Pharmaceuticals Inc. filed for an initial public offering, hoping to raise \$172.5 million to support commercialization of Luvox CR, an approvable drug for psychiatric disorders, and continued development of other pipeline products.

The Palo Alto, Calif.-based company has not yet determined the share price or number of shares to be offered. Upon completion of the offering, its stock would trade on Nasdaq under the ticker "JAZZ."

Founded in 2003 to develop drugs for neurological and psychiatric disorders, Jazz works to enhance known compounds using new formulations and drug delivery approaches. The company gained its first marketed products via its April 2005 acquisition of Minnetonka, Minn.-

See Jazz, Page 7

INSIDE: NEWS FROM WASHINGTON: FDA APPROVALS3
APPOINTMENTS AND ADVANCEMENTS4, 7



OTHER NEWS TO NOTE

• **Active Biotech AB**, of Lund, Sweden, reported positive data from a Phase Ib study of TASQ, an oral agent being developed to treat prostate cancer. The Swedish study in hormone-refractory patients showed five of six patients had a decrease in prostate-specific antigen velocity of more than 50 percent compared to prior treatment. Three of the five patients exhibited a decrease in absolute PSA levels. The study also demonstrated safety of 1 mg/day of TASQ, double the previously reported maximum tolerated dose. Phase II studies are scheduled to start sometime this year.

• **Bio-Bridge Science Inc.**, of Oak Brook, Ill., signed a cooperative agreement with the Chinese Academy of Medical Sciences to develop a human papillomavirus vaccine expected to provide broader protection than Gardasil (Quadrivalent Human Papillomavirus [Types 6, 11, 16, 18] Recombinant Vaccine, Merck & Co. Inc.) with lower production costs. Bio-Bridge has assumed a 60 percent interest in the project and will receive preferential right to develop the vaccine. Bio-Bridge also is developing an HIV vaccine in cooperation with the Beijing Institute of Radiation Medicine.

• **F. Hoffmann-La Roche Ltd.**, of Basel, Switzerland, filed a supplemental new drug application to market 30-mg and 45-mg pediatric doses of Tamiflu (oseltamivir phosphate), which was co-developed by **Gilead Sciences Inc.**, of Foster City, CA. Tamiflu currently is available in a 75-mg capsule for adults and a liquid suspension formulation for children, but the lower-dose capsules have a longer shelf life than the liquid and may appeal to the government for stockpiling efforts. Roche anticipates an FDA decision by mid-2007. Also on Friday, the UK's National Institute for Health and Clinical Excellence said it will not make Tarceva (erlotinib, Roche and Genentech Inc. and OSI Pharmaceuticals Inc.) available on the National Health Service for the

treatment on non-small-cell lung cancer. Roche said it will appeal the ruling.

• **IGI Inc.**, of Buena, N.J., said that Kearny, N.J.-based **Pharmachem Laboratories Inc.** made an equity investment of \$1.5 million by purchasing 1.5 million shares of IGI's common stock. Those funds will be used to repay outstanding debts and accrued interest, as part of IGI's efforts to comply with requirements for its continued listing on the American Stock Exchange. The company previously signed an agreement for a \$1 million line of credit with Pharmachem, though it cancelled that arrangement in favor of an 18-month, \$1 million revolving line of credit with Pinnacle Mountain Partners LLC. IGI manufactures dermatological, consumer, skin care and hair care products for third parties using the Novasome lipid vesicle encapsulation technologies licensed from Malvern, Pa.-based **Novavax Inc.**

• **Innogenetics NV**, of Ghent, Belgium, said the U.S. Court of Appeals denied a motion by **Abbott Laboratories**, of Abbott Park, Ill., for a stay of an injunction pending appeal. The ruling overturned a temporary stay ruling from Jan. 19. Innogenetics successfully sued Abbott in September 2005, alleging Abbott was infringing a patent covering a method of genotyping the hepatitis C virus. Jan. 4, a judge dismissed Abbott's requests for a new trial, affirmed the jury's finding that the patent was valid in all respects and approved the award of \$7 million in damages. Jan. 10, the judge granted Innogenetics' request for a permanent injunction, enjoining Abbott from any further sales or other uses that would infringe on the Innogenetics' technology.

• **Pressure BioSciences Inc.**, of West Bridgewater, Mass., received its second Phase I Small Business Innovation Research grant (SBIR) from the National Institutes of Health. The grant is for \$150,000 over six months, and follows a six-month, \$150,000 SBIR grant received last October. Funds will be used to demonstrate the feasibility of using the company's Pressure Cycling Technology to develop a novel, automated sample preparation procedure for the extraction and purification of nucleic acids from a variety of biological samples in a single processing step.

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*News From Washington***Looking Back, FDA Approvals Continue To Trend Down In '06****By Aaron Lorenzo**
Washington Editor

WASHINGTON – According to a recently released document, the FDA approved 32 new molecular entities last year, a downturn from 2005's 38 approvals that continues a trend of fewer new product clearances in recent years.

The agency's Center for Drug Evaluation and Research (CDER) cleared the majority of the new products, including 18 new drug applications and four biologic license applications. Ten were priority products approved in six months, on average, and 12 were standard reviews approved in the median time of 13.7 months.

The FDA's Center for Biologics Evaluation and Research (CBER) approved 10 new BLAs. Three received priority reviews and were cleared within 6.4 months, on average, and the remainder were approved in an average standard time frame of 13 months.

Among products approved last year were a few antibodies, including Lucentis (ranibizumab, Genentech Inc.) for wet age-related macular degeneration, Sprycel (dasatinib, Bristol-Myers Squibb Co.) for several types of leukemia and Sutent (sunitinib malate, Pfizer Inc.) for gastrointestinal tumors and advanced kidney cancer. New enzyme replacement therapies include Myozyme (alglucosidase alfa, from Genzyme Corp.) for Pompe disease and Elaprase (idursulfase, from Shire plc) for Hunter Syndrome. New vaccines include FluLaval (GlaxoSmithKline plc) for influenza and Gardasil (Merck & Co. Inc.), a vaccine against human papillomavirus to prevent cervical cancer. In addition, the angina drug Ranexa (ranolazine, CV Therapeutics Inc.) received approval.

According to the FDA, CDER approved 20 new molecular entities in 2005 and CBER cleared 18 BLAs.

Anti-Human Cloning Bill Introduced

Sens. Orrin Hatch (R-Utah) and Dianne Feinstein (D-Calif.) last week reintroduced legislation that would prohibit the cloning of a human being but allow somatic cell nuclear transfer for therapeutic purposes to continue.

The bill, "The Human Cloning Ban and Stem Cell Protection Act of 2007," or S. 812, is written to allay critics' fears

that the embryonic stem cell technique could be used for unethical purposes. In particular, the framework establishes stiff civil penalties for abusing somatic cell nuclear transplantation: The measure criminalizes human cloning, punishable by up to 10 years in prison, without exception, along with fines of \$1 million or three times any profits made on anyone who clones or attempts to clone a human being, whichever sum is greater.

The legislation is co-sponsored by Sens. Edward Kennedy (D-Mass.), Arlen Specter (R-Pa.) and Tom Harkin (D-Iowa). All also are strong supporters of a bill to expand the number of embryonic stem cell lines eligible for federal backing, "The Stem Cell Research Enhancement Act of 2007," or S. 5. It has yet to come to the Senate floor for a vote, but the lawmakers earlier this year indicated that action would be taken this spring.

Companion legislation in the House of Representatives, H.R. 3, cleared a floor vote early this year, 253-174. (See *BioWorld Today*, Jan. 16, 2007.)

Off-Label Limits Worry Gottlieb

Former FDA official Scott Gottlieb last week penned an op-ed in the *Wall Street Journal* warning that federal government distrust of doctors' off-label prescribing practices could have deleterious effects on patients.

Strict limits on such treatment could result from pending legislation from Sens. Kennedy and Mike Enzi (R-Wyo.), whose bill would mandate risk-management plans for all drugs on the market instead of those the FDA deems in need of caution. Gottlieb, now a resident fellow at the American Enterprise Institute, also cautioned against prescribing limits imposed by the Department of Justice and the Centers for Medicare & Medicaid Services.

Echoing a speech he made in December, Gottlieb said any approach that imposes "one-size prescriptions in an area of science that is marked by variation" would harm patients.

His words were published Tuesday, a day after the House Committee on Oversight and Government Reform, chaired by Rep. Henry Waxman (D-Calif.), notified several drug and device makers that an investigation had been opened into allegations of inappropriate marketing and off-label promotions on their part.

He requested they respond with a range of documents by March 21. ■



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Amgen

Continued from page 1

mittee meeting to further discuss EPO drug issues. Pazdur said regulators are looking more closely at the whole class.

New warnings also will apply to EPO drugs that the FDA has yet to approve, including continuous EPO receptor activator from Switzerland-based F. Hoffmann-La Roche Ltd., which could mean delays beneficial to Amgen.

Amgen's shares (NASDAQ:AMGN) dipped \$1.31 on Friday, to \$60.86, on word that updated label information lets patients know of death risks plus chances of cardiovascular events and tumor growth when the erythropoietin products are used in off-label dose regimens or populations.

All three drugs are approved to treat anemia in chronic kidney failure patients and those on chemotherapy for cancer. Epogen (epoetin alfa) and its counterpart Procrit, marketed by New Brunswick, N.J.-based Johnson & Johnson, also are cleared for patients scheduled for major surgery to reduce blood transfusions and for anemia in certain HIV patients.

According to the new warning, the drugs – when given to target a hemoglobin level of >12 g/dL – boosted the risk of death and cardiovascular events, cut the time to tumor progression in patients with advanced head and neck cancer who got radiation therapy and shortened overall survival while hiking deaths because of disease progression at four months in metastatic breast cancer patients getting chemo.

Death risk also went up, according to the warning, when the anemia-therapies were given to target a hemoglobin of 12 g/dL in patients with active malignant disease who are not getting chemo or radiation. That's a nonapproved use. Another group included in the warning is pre-operative patients who want to reduce allogeneic blood transfusions and are not already on clotbusters.

Thousand Oaks, Calif.-based Amgen's label specifies starting treatment at hemoglobin levels <12 g/dL, withholding therapy if they reach 13 g/dL and continuing the drug at levels <13 g/dL.

Some had worried that Aranesp (darbepoetin alfa) is given to patients with hemoglobin >13 g/dL, or begun at levels >12 g/dL, but Amgen's claim to the contrary won backing from a data query of about 1,100 electronic medical records collected by Supportive Oncology Services, an information company in Memphis, Tenn.

The data, included in a report by Robert Baird & Co. in Chicago, show that mean hemoglobin levels at the first Aranesp treatment is 10.2 g/dL, and mean levels at subsequent dosing is 10.8 g/dL. Patients who began treatment with >12 g/dL proved minimal in the survey (1.9 percent), and only 2.3 percent of subsequent doses were given to patients with >13 g/dL. Similar numbers had been offered by Amgen, showing 98 percent of patients begin treatment at <12 g/dL and only 97 percent are treated again with >13 g/dL.

"With this negligible off-label use in chemotherapy-induced anemia, we believe tighter FDA language regarding hemoglobin maintenance would have little effect on [sales]," wrote analyst Chris Raymond in the Baird report.

Bret Holley with CIBC World Markets in New York did not see much consequence in the label change, either, since they reflect findings in studies already disclosed. He allowed that "there could be some incremental reductions in overall EPO usage over the longer term," plus dosing vigilance and limits in the cancer-anemia setting. But Amgen's stock value "may be overly discounting doomsday scenarios" for EPO drugs, "given the totality of historical safety data and physician experiences with the drugs."

Pazdur said doctors generally would target hemoglobin levels of 10 g/dL. The changed label language reflects a revision to past thinking that "more is better" in terms of dosing, explained Karen Weiss, the oncology office's deputy director.

Verbiage also has been stripped from the products' labels for cancer use with regard to improving fatigue and other patient-reported outcomes. The FDA will further review quality-of-life claims in the kidney disease setting before determining whether to make any changes there. Meanwhile, a "dear doctor" letter will inform physicians of the changes.

Fourth-quarter 2006 worldwide sales of Aranesp hit about \$1.1 billion, a 27 percent increase over the period last year. Full year sales reached \$4.1 billion, a 26 percent increase over 2005. Epogen sold \$661 million during the quarter, which marked an increase of 6 percent, partly offset by the growing use of Aranesp (the second-generation Epogen) in hospitals. ■

APPOINTMENTS AND ADVANCEMENTS

Acacia Research Corp., of Newport Beach, Calif., has appointed Mansoor Mohammed president and CEO of its CombiMatrix Molecular Diagnostics Inc. subsidiary.

Acusphere Inc., of Watertown, Mass., has named Howard Bernstein executive vice president of research and development; Donald Chickering vice president of technical operations; and Julie Straub executive director of research.

Alba Therapeutics Corp., of Baltimore, has appointed Linda M. Arterburnas its senior director of in vivo pharmacology and toxicology.

Alfancell Corp., of Bloodfield, N.J., has appointed Michael S. Kinch to its scientific advisory board.

Alkermes Inc., of Cambridge, Mass., has named David A. Broecker, current president, as president and chief operating officer. Current CEO Richard F. Pops will become chairman of the board of directors.

Bioponic Phytoceuticals Inc., of Kula, Hawaii, has named Richard Alpert to its board of directors.

Neose

Continued from page 1

share. Neose said it would file a registration statement for the securities by May 15. Neose's stock (NASDAQ:NTEC) were down 7 cents Friday to close at \$1.89.

Neose said the securities were being purchased by institutional investors and investment funds affiliated with directors.

Among the uses for the money will be to support development of NE-180, which in January began Phase II development in Switzerland for treatment of chemotherapy-induced anemia. NE-180 is a GlycoPEGylated erythropoietin agent designed to have an improved therapeutic profile, including a longer half-life, compared to non-pegylated EPO.

A Phase II trial of NE-180 for treating anemia associated with chronic kidney disease was expected to begin this year. Development of the product in the U.S. has been on hold pending resolution of FDA questions about assay potency.

Company officials were not available for comment, but were expected to provide updates on Neose programs when they release fourth-quarter earnings this week.

The other clinical-stage program at Neose is GlycoPEG-GCSF, a long-acting version of granulocyte-colony stimulating factor. Partner BioGeneriX AG, of Mannheim, Germany, is testing the G-CSF product for neutropenia in a Phase I trial in Europe, a study comparing the agent to Amgen Inc.'s Neulasta (pegfilgrastim).

Late last year BioGeneriX, a Ratiopharm Group company, said it would exercise its option to continue development of GlycoPEG-GCSF. Neose retains rights in North America and Japan. At the same time, BioGeneriX declined its option to develop a pegylated EPO program made in Chinese hamster ovary cells. (NE-180 is made in an insect cell-based expression system.)

Neose also has a partnership with Novo Nordisk A/S, of Bagsvaerd, Denmark, which is using the GlycoPEGylation technology to develop next-generation versions of Factors VIIa, VIII and IX for bleeding episodes, hemophilia A and hemophilia B, respectively. Neose received \$4.3 million up front under the November 2003 deal, and is entitled to up to \$51.3 million in milestone payments. Neose also would get royalties on resulting sales.

Neose has programs in the research stage on GlycoPEGylated products incorporating human growth hormone, for growth hormone deficiency, and interferon alpha, for hepatitis C.

In its 10-Q filing in November, Neose had estimated its cash on hand of \$23.6 million at the end of September would fund operations at least through this quarter, so the new funding gives the company some breathing room.

Its loss in the third quarter was only \$1.4 million, but that included one-time gains related to the sale of a facility containing its headquarters and a pilot manufacturing

plant, and the recognition of charges from an August 2005 restructuring. Its net loss for the nine months ending Sept. 30 was \$17.6 million.

Neose' enzymatic GlycoAdvance and GlycoPEGylation technologies are designed to improve properties of therapeutic proteins by building out, and attaching polyethylene glycol to, carbohydrate structures on the proteins. It said the modified proteins could offer significant advantages to the original version, including less frequent dosing and, potentially, improved efficacy. ■

OTHER NEWS TO NOTE

• **Protalix BioTherapeutics Inc.**, of Carmiel, Israel, said its stock was approved for listing on the American Stock Exchange. It is expected to begin trading on AMEX shortly under the symbol "PLX." The stock has been trading over the counter. The move followed the Jan. 3 completion of the merger between Protalix and the Miami-based public shell company **Orthodontix Inc.** That deal originally was announced in August. Protalix's technology is based on its plant cell culture and bioreactor system for industrial production of recombinant biopharmaceuticals.

• **Scolr Pharma Inc.**, of Bellevue, Wash., revealed that its previously undisclosed partner in the development of an oral formulation of a promising antiviral flu compound is **BioCryst Pharmaceuticals Inc.**, of Birmingham, Ala. The companies are using Scolr's CDT drug delivery platform to develop an oral version of peramivir to treat and prevent various types of flu. An intramuscular formulation of peramivir is in Phase II, and BioCryst recently received a \$102.6 million contract from the U.S. Department of Health and Human Services to develop the drug for the treatment of seasonal and life-threatening influenza, including avian flu. Japanese rights have been licensed to **Shionogi & Co. Ltd.**, of Osaka, Japan, in a \$130 million deal. (See *BioWorld Today*, Jan. 5, 2007 and March 7, 2007.)

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Ceregene

Continued from page 1

use neuronal growth factors to treat neurodegenerative diseases. The idea was to slow and maybe repair the damage, regardless of underlying cause.

Unfortunately, all of those programs were dropped, in some cases after running several Phase III trials. Nobody could deliver enough of the factors in a selective way to the correct location to drive reproducible, significant clinical improvement. Some unexpected toxicity showed up – probably because of delivery problems.

Amazingly, neuronal growth factors are back in the clinic with big bucks behind them. The key to the rebirth? A new approach that more closely mimics natural delivery of those factors.

Ceregene was launched in 2001 as a subsidiary of Cell Genesys, getting a nice dowry of \$10 million plus IP. Cell Genesys CEO Steve Sherwin and his team saw an opportunity to keep an internal focus on cancer therapies, while pursuing CNS gene therapy in a focused way. (Sherwin's team likes spinouts as a mechanism for generating value. They spun out Abgenix with its human monoclonal antibody technology in 1996. Abgenix went public in 1998 and was bought for \$2.2 billion by Amgen in 2006.)

Another important ingredient was Neurological Gene Therapeutics (NGT), a virtual start-up founded by Mark Tuszynski and Armin Blesch of University of California – San Diego, and Jeffrey Kordower of the Research Center for Brain Repair at Rush Presbyterian in Chicago.

Tuszynski was trying to figure out how to get nerve growth factor (NGF) into cholinergic nerves in the desired brain region in Alzheimer's patients. His UC-SD team used ex vivo NGF gene therapy and reimplantation to reverse age-related neuronal atrophy in monkeys, restoring normal numbers and activity of axons.

Ceregene in-licensed that technology, and in 2001, Tuszynski treated skin cells from Parkinson's patients ex vivo with the NGF gene therapy and reimplanted them in the damaged brain region with stereotactic injection. Responding patients had a 50 percent reduction in the rate of decline and enhanced brain activity, measured by PET-glucose metabolism. Two years later, those patients still showed improvement.

But the 1990s convinced many that ex vivo cell therapy was a scary business model. The new Ceregene team created an AAV vector carrying the NGF gene, delivered by a proprietary in vivo procedure. A 2001 Phase I study in six patients showed promising results in line with the ex vivo treatment.

CEO Jeff Ostrove said Ceregene wants a partner to help support the Phase II trial – 50 patients, double-blind, 24 months duration, \$5 million. Ostrove said they would love to team up with someone other than a conventional corporate partner and retain the product rights. (Hey, Symphony Capital, are you listening?)

But even more promising were rat studies showing that a single treatment in vivo with an adeno-associated

virus (AAV) vector carrying the glial-derived neurotrophic factor (GDNF) gene was able to restore nerve function in a rodent model of Parkinson's.

Parkinson's Program

Amgen, owner of the GDNF patents and pursuing it until 2005, didn't want to license the gene to Ceregene, so the team switched to neurturin, a cousin of GDNF, delivered by needle directly into the brain site affected by Parkinson's.

Unlike previous methods – infusion into ventricles or a canula in the striatum – Ceregene's delivery is designed to mimic natural expression in the striatum. The AAV vector, which expresses no viral proteins, requires only 80 microliters, vs. the milliliters used in ventricle delivery approaches. The company believes that with less volume and less viral particles, there is less concern for immune reaction. Bonus point – you need only 10,000 square feet of manufacturing to make enough drug for the entire Parkinson's market.

The preclinical studies showed that approach to be lacking the adverse effects seen with ventricle delivery. Neurturin expression starts in 2 days, peaks at day 28 and persists at least 24 months.

In an open-label single-treatment Phase I, 12 patients showed a 40 percent ($p < 0.001$) reduction in symptoms. Ceregene began Phase II early this year that will treat 51 patients for 12 months, with a crossover for another 24 months to look for persistence of treatment effects. The Michael J. Fox Foundation providing partial financial support for both trials.

A New Route Of Delivery

Ceregene's delivery approach is easily extended to other neurodegenerative diseases. After Cephalon and Chiron gave up on IGF-1 for ALS in 1998, Fred Gage's mouse studies at Salk suggested that retrograde transport of the AAV construct up peripheral nerves might be a more successful route of delivery. Ceregene licensed the technology and Project ALS, the ALS Association, the Robert Packard Foundation and NIH are funding the program. Ceregene has some early programs in Huntington's disease and retinal disorders, both based on preserving neural cell function.

Ostrove said that Ceregene is a development company, working with well-established factors that were discovered and cloned by others, and in-licensed by Ceregene. The novel twist is finding a solution to the delivery challenges that stymied earlier programs.

That appealed to Alta, MPM, California Technology Ventures and Hamilton BioVentures, who put in another \$32 million in 2004. Cell Genesys retained a 25 percent stake in Ceregene. A series C round is in the works.

Will Ceregene succeed where others failed after expending significant time, energy and resources? For the sake of those patients, we certainly hope so.

Robbins-Roth, PhD, founding partner of BioVenture Consultants, can be reached at biogodess@earthlink.net. Her opinions do not necessarily reflect those of BioWorld Today. ■

Jazz

Continued from page 1

based Orphan Medical Inc., most notably Xyrem (sodium oxybate oral solution) for cataplexy and daytime sleepiness in narcolepsy patients.

Sales of Xyrem accounted for more than half of the company's \$41.9 million revenue in 2006. (See *BioWorld Today*, April 20, 2005.)

In its prospectus, Jazz said proceeds from the IPO would support the commercial launch for Luvox CR (fluvoxamine maleate extended-release capsules), a selective serotonin reuptake inhibitor licensed in January from Marietta, Ga.-based Solvay Pharmaceuticals Inc. The product was deemed approvable last month for treating obsessive compulsive disorder and social anxiety disorder. Pending approval, Jazz expects to begin promoting Luvox CR in the U.S. in early 2008, at which time it plans to more than double its 55-person sales force.

A portion of funds also would be used for ongoing development of the company's clinical pipeline, which includes JZP-6, a liquid dosage form of Xyrem that is in two pivotal Phase III studies in fibromyalgia syndrome (FMS). Preliminary results from the first of those trials are expected in the second half of 2008. Xyrem's European marketing partner, UCB SA, of Brussels, Belgium, also has rights to JZP-6 in FMS.

Jazz intends to start Phase II studies this year with JZP-4, a Type IIa sodium channel antagonist for epilepsy and bipolar disorder, and with JZP-8, a formulation incorporating benzodiazepine for treating acute repetitive seizure clusters in refractory epilepsy patients. Earlier in the pipeline, the company has JZP-7, a dopamine agonist, which will be evaluated in an additional pharmacokinetics study later this year before beginning Phase II studies in restless legs syndrome. A fast-acting version of benzodiazepine, JZP-2, is expected to enter the clinic in 2007 as an acute treatment of panic attacks associated with panic disorder.

Any remaining proceeds will be put toward working capital, capital expenditures and general corporate purposes.

Jazz, which reported a net loss of \$59.4 million for 2006, ended the year with cash and cash equivalents totaling \$78.9 million. The company said that those funds, combined with the IPO proceeds, plus anticipated revenues and royalties from product sales, should sustain operations for at least the next 12 to 18 months.

As of Dec. 31, Jazz had 205.2 million shares outstanding. Its principal stockholders consist of funds affiliated with several investment groups, including Kohlberg Kravis Roberts & Co. LP, which holds 98.1 million shares, or about 48 percent of the company; Thoma Cressey Bravo Inc., with 22 million shares, or 11 percent; Beecken Petty O'Keefe & Co., with 14.7 million shares, or 7 percent; Prospect Venture Partners and Versant Ventures, each of which owns 13.7 million shares, or almost 7 percent; Golden Gate Capital,

with 11 million shares, or 5 percent; and Lehman Brothers Holdings Inc., with 10.7 million shares, or 5 percent.

Morgan Stanley, Credit Suisse, Lehman Brothers and Natexis Bleichroeder Inc. are acting as underwriters for the offering. ■

APPOINTMENTS AND ADVANCEMENTS

Biosite Inc., of San Diego, has named Thomas Blassey vice president, U.S. sales.

Caden Biosciences, of Madison, Wis., has appointed William Clarke, CEO of Celectar LLC, to its board.

Canaccord Adams, of Boston, has named Jeff Barlow managing director and head of life sciences banking; Matt Steere managing director; and William Plovanic and Jason Mills managing directors in equity research.

Cardiome Pharma Corp., of Vancouver, British Columbia, has named Don McAfee chief scientific officer, and Karim Lalji to the position of senior vice president of commercial affairs.

Cortex Pharmaceuticals Inc., of Irvine, Calif., has named Les Street head of medicinal chemistry, and Steven A. Johnson an officer of the company.

Elbion NV, of Leuven, Belgium, has appointed Koenraad Blot chief medical officer.

Epiphany Biosciences Inc., of San Francisco, has appointed virologist Michael Houghton chief scientific officer.

Hana Biosciences, of South San Francisco, has appointed Lyn Wiesinger to its board of directors.

Immunotope Inc., of Doylestown, Pa., has appointed Edward L. Erickson and Elizabeth E. Tallett to its board of directors.

Innovive Pharmaceuticals Inc., of New York, has appointed Angelo De Caro to its board of directors and audit committee.

Invitrogen Corp., of Carlsbad, Calif., has appointed Per Peterson to its board of directors.

Lexicon Genetics Inc., of The Woodlands, Texas, has named Brian P. Zambrowicz executive vice president and chief scientific officer. It also named Alan J. Main executive vice president of pharmaceutical research, and elected Kathleen Wiltsey to its board of directors.

Med BioGene Inc., of Vancouver, British Columbia, has appointed Richard C. Cook, to its scientific advisory board.

Oncologic Inc., of Berkeley, Calif., has named Stephen Isaacs president and CEO.

OncoMed Pharmaceuticals, of Redwood City, Calif., has appointed Steven E. Benner to the position of senior vice president and chief medical officer.

Oramed Pharmaceuticals Inc., of Jerusalem, has appointed three new members to its board: Ele Ferrannini, Derek LeRoith and Itamar Raz.