

BIOWORLD® TODAY

WEDNESDAY
MAY 23, 2007

THE DAILY BIOTECHNOLOGY NEWSPAPER

VOLUME 18, No. 100
PAGE 1 OF 9

QuatRx Boosts Pipeline Work With \$44M Series E Financing

By Jennifer Boggs
Staff Writer

In its largest financing round to date, QuatRx Pharmaceuticals Co. brought in \$44 million in a Series E round to support ongoing clinical development of two endocrine programs, including a Phase III-stage selective estrogen receptor modulator for vaginal atrophy, and an early clinical-stage lipid-lowering compound.

The Ann Arbor, Mich.-based firm has raised a total of \$122 million since it began operations in 2002. QuatRx had intended to gain a public listing last year, filing for an \$86 million initial public offering in February 2006, but instead, became one of several companies to reconsider due to unfavorable market conditions. Fortunately, for QuatRx, the venture capital markets have remained receptive.

"We have a very strong portfolio" of candidates for
See QuatRx, Page 3

Financings Roundup

Genomic Health Raises \$46.5M For Personalized Diagnostics

By Jim Shrine
Staff Writer

Genomic Health Inc. raised \$46.5 million in a public offering to fund development and expansion of its genomics-based clinical diagnostic tests in cancer applications.

The Redwood City, Calif., company sold 3 million shares at \$15.50 per share. Underwriters have an option to purchase up to 450,000 additional shares to cover over-allotments. Genomic Health's stock (NASDAQ:GHDX) gained 89 cents Tuesday, or 5.1 percent, to close at \$16.58.

Genomic Health in 2004 launched its first test, Oncotype DX, which is used to predict the likelihood of cancer recurrence, the likelihood of patient survival within 10 years of diagnosis and the likelihood of chemotherapy benefit in early stage breast cancer patients. The company,
See Financings Roundup, Page 4

Wnt Strikes Again

New Alzheimer's Avenues In Targeting Of Amyloid, Tau

By Anette Breindl
Science Editor

Elan Corp plc and Wyeth generated much excitement with yesterday's announcement of their plan to begin Phase III testing of bapineuzumab (AAB-001) for mild to moderate Alzheimer's disease later this year. (See *BioWorld Today*, May 22, 2007.)

Bapineuzumab targets amyloid beta, as do the majority of therapeutic agents that currently are in clinical development. Clumps of misfolded amyloid beta protein, known as amyloid plaques, are one of the cellular hallmarks of Alzheimer's disease, making them natural targets. Recent studies suggested a new way to manipulate amyloid beta levels, as well as an avenue for taking on Alzheimer's independently of amyloid beta.

See Alzheimer's, Page 5

Orexigen Starts Second Of Four Phase III Trials Of Obesity Drug

By Aaron Lorenzo
Washington Editor

Fresh out of its post-IPO quiet period, Orexigen Therapeutics Inc. has a lot to say about its obesity drug Contrave, a fixed-dose product that combines sustained-release formulations of bupropion and naltrexone. The San Diego biopharmaceutical company, which last month completed an \$84 million initial public offering, has just moved Contrave into the second of four Phase III studies in hopes of eventually entering a developing landscape of medicines to address the growing problem.

"The market's size, the level of dissatisfaction and a significant consumer insight and interest in therapeutic alternatives," said Orexigen President and CEO Gary Tollefson, "all speak to why there is so much commercial interest in products in the obesity space."

See Orexigen, Page 6

INSIDE: BIOSEEK'S AMYLIN DEAL GETS \$10M	2
CLINIC ROUNDUP	3, 5-7



BioSeek's Amylin Deal Gets \$10M For Inflammation Work

By **Randall Osborne**
West Coast Editor

BioSeek Inc.'s addition of Amylin Pharmaceuticals Inc. to the partner list puts \$10 million into the coffers for its own program, as the firm carries out research with Amylin on the potential of peptides against inflammatory disease.

For BioSeek, the investment represents a fair bit of cash, considering the firm has raised \$19 million total since its inception in 2000, said Peter Staple, CEO of the Burlingame, Calif.-based firm. BioSeek will apply its BioMAP screening system to Amylin's polypeptide hormone library, called Phormol.

"This screening deal gives us the right to pick the top two [peptides] that we're interested in, and we get to take those forward," Staple said, while metabolics-focused Amylin gets data on the rest. Milestone payments would be due Amylin, along with royalties on any products resulting. The pact builds on an agreement first made in 2006, and gives BioSeek access to Amylin's chemistry expertise.

BioSeek's BioMAP is made of a series of human primary cell-based assay systems to characterize existing lead compounds and identify new ones. If Amylin develops or licenses an additional limited set of peptides for the uses specified in the arrangement, BioSeek could get royalties as well.

Other BioSeek partners include London-based GlaxoSmithKline plc and Inflazyme Pharmaceuticals Ltd., of Vancouver, British Columbia. The latter signed last June to have BioSeek profile the mechanisms of action of Inflazyme's leukocyte selective anti-inflammatory drugs (LSAIDs) for respiratory illness.

Inflazyme's recent Phase IIb fizzle of IPL512,602, an LSAID for asthma, was blamed on a surprisingly large placebo response. Clinical failure is what BioMAP screening aims to help partners avoid, but Staple declined to say whether the work for Inflazyme involved IPL512,062.

"I can't really comment on the results," he said, and

pointed to the possibility that Inflazyme "may want to come back for more" work.

BioSeek has done between 25 and 30 collaborative deals, Staple said. "With many partners, we've done follow-up programs, and we're working on extended collaborations with a number of companies," he said.

Other BioSeek partners include Boston Scientific Corp., of Natick, Mass., and Berkeley, Calif.-based Dynavax Technologies Corp. For Dynavax, BioSeek used BioMAP on a family of TNF-alpha inhibitors, known as thiazolopyrimidines, on which Dynavax is conducting research for chronic inflammatory diseases.

Alice Bahner, director of investor relations for San Diego-based Amylin, acknowledged that the agreement with BioSeek is "a different direction" for the firm, but officials have "talked about the possibility of our peptide library being used in different disorders," and the collaboration echoes a deal made earlier this year with PsychoGenics Inc., of Tarrytown, N.Y. With PsychoGenics, Amylin has formed a new company, called Psylin Neurosciences Inc, which will mine Phormol for potential compounds to treat central nervous system disorders. (See *BioWorld Today*, Jan. 31, 2007.)

"We've been working on Phormol for quite some time, but we've just recently begun exploring the potential," Bahner said. Amylin developed and sells the injectables Symlin (pramlintide) and Byetta (exenatide) for diabetes. Byetta brought in \$147 million in the first quarter, and Symlin added \$15.5 million to revenues for the period. ■

ADVERTISE HERE

...and reach high-level biotechnology professionals every day!

For advertising opportunities in
BioWorld Today, please contact
Stephen Vance at (404) 262-5511
or stephen.vance@ahcmedia.com

BioWorld® Today (ISSN# 1541-0595) is published every business day by AHC Media LLC, 3525 Piedmont Road, Building Six, Suite 400, Atlanta, GA 30305 U.S.A. Opinions expressed are not necessarily those of this publication. Mention of products or services does not constitute endorsement. BioWorld® and BioWorld® Today are trademarks of AHC Media LLC, a Thompson Publishing Group company. Copyright © 2007 AHC Media LLC. All Rights Reserved. No part of this publication may be reproduced without the written consent of AHC Media LLC. (GST Registration Number R128870672).

ATLANTA NEWSROOM: Managing Editor: **Glen Harris**.
Staff Writers: **Jennifer Boggs, Trista Morrison, Jim Shrine**.
Senior Production Editor: **Ann Duncan**. Editorial Coordinator: **Tiffany Turner**.

WASHINGTON BUREAU: Washington Editor: **Aaron Lorenzo**.

WEST COAST BUREAU: Editor: **Randall Osborne**.

EAST COAST BUREAU: Science Editor: **Anette Breindl**.

BUSINESS OFFICE: Senior Vice President/Group Publisher: **Donald R. Johnston**.
Senior Marketing Product Manager: **Chris Walker**.
Account Representatives: **Steve Roberts, Bob Sobel, Chris Wiley**.

DISPLAY ADVERTISING: For ad rates and information, please call **Stephen Vance** at (404) 262-5511 or email him at stephen.vance@ahcmedia.com.

REPRINTS: For photocopy rights or reprints, call our reprints department at (404) 262-5479.

PRESS MATERIALS: Send all press releases and related information to newsdesk@bioworld.com.

SUBSCRIBER INFORMATION

Please call **(800) 688-2421** to subscribe or if you have fax transmission problems. Outside U.S. and Canada, call **(404) 262-5476**. Our customer service hours are 8:30 a.m. to 6:00 p.m. EST.

Glen Harris, **(404) 262-5408**

Aaron Lorenzo, **(202) 739-9556**

Jennifer Boggs, **(404) 262-5427**

Jim Shrine: **(404) 627-2621**

Fax: **(404) 814-0759**

Randall Osborne, **(415) 384-0872**

Anette Breindl, **(304) 296-1160**

Trista Morrison, **(858) 901-4785**

Senior Vice President/Group Publisher:
Donald R. Johnston, (404) 262-5439

Internet: <http://www.bioworld.com>



AHC Media LLC

QuatRx

Continued from page 1

endocrine, metabolic and cardiovascular disorders, said Gary Onn, the company's chief financial officer, and those candidates are "targeting large markets, in excess of \$1 billion a year."

QuatRx's lead candidate, Ophena, is in development for postmenopausal symptoms in women, leading off with vaginal atrophy. An oral SERM, Ophena is aimed to be an alternative to traditional hormone replacement therapies, which in 2004 totaled about \$1.7 billion in U.S. sales. In early studies, Ophena demonstrated an ability to mimic estrogen's action in bone tissue without stimulating estrogen's effects in the breast and uterus that can increase cancer risk.

The company expects "to see data from that first Phase III trial around the end of 2007," Onn told *BioWorld Today*. Pending positive results, a second Phase III study is planned to start in 2008, with a new drug application anticipated around the end of 2009.

Behind Ophena is a second endocrine product, fispemifene, a selective estrogen receptor antagonist in development for testosterone deficiency in men. The product is designed to "elevate testosterone levels to the normal range by using the body's own mechanisms," Onn said. Fispemifene is in Phase II studies.

QuatRx gained rights to both Ophena and fispemifene through its May 2005 acquisition of Finnish firm Hormos Medical Ltd. (See *BioWorld Today*, May 17, 2005.)

The company also has QRX-431, a selective thyroid beta agonist that demonstrated in preclinical studies an ability to lower LDL without significant heart rate increases. That product is in Phase I testing, and results from a multiple-dose study should be available around the end of the year, Onn said.

QuatRx owns rights to all three products. Though it likely will seek commercialization partners to reach those large markets, Onn said the company plans eventually to build its own sales force and establish its own marketing efforts.

Earlier this month, the company out-licensed a fourth product in its development pipeline, a psoriasis drug that fell outside the company's focus of endocrine, metabolic and cardiovascular diseases. In that deal, Newtown, Mass.-based CollaGenex Pharmaceuticals Inc. paid QuatRx a \$1.5 million licensing fee for rights to develop and commercialize becalcidiol, a vitamin D analogue in Phase II trials as a topical psoriasis treatment. QuatRx also is eligible to receive undisclosed development and sales milestones, as well as royalties on any resulting sales.

With the latest funding round, the company should have sufficient money to operate for "about the next 18 months," Onn said. In the meantime, QuatRx might contemplate another run at a public listing if the market improves.

"We always have an eye on the public market," Onn said, "but right now, our plan is just to advance the portfolio. We might take a look at the public markets again early next year."

The Series E round was led by new investor Menlo Park, Calif.-based Venrock, and Venrock partner Anders Hove joined the company's board. Other new investors Baltimore-based T. Rowe Price; Stockholm, Sweden-based Catella Healthcare; and Palo Alto, Calif.-based Hercules Technology Growth Capital also participated, along with a number of existing investors, including: Frazier Healthcare Ventures, of Seattle; TL Ventures, of Wayne, Pa.; MPM Capital, of Boston; InterWest Partners, of Menlo Park, Calif.; Thomas Weisel Healthcare Ventures, of Palo Alto, Calif.; Stockwell Capital, of Chicago; H&B Capital, of Stockholm; BioMedical Ventures, of Copenhagen, Denmark; Bio Fund Ventures, of Helsinki, Finland; and Twilight Venture Partners, of Indianapolis.

Aquilo Partners Inc. served as the exclusive placement agent for the financing. ■

CLINIC ROUNDUP

- **Auxilium Pharmaceuticals Inc.**, of Malvern, Pa., said retrospective data reported at the American Urological Association meeting in Anaheim, Calif., showed improvements in symptoms of decreased libido, energy levels and erectile function in 76 percent of hypogonadal men after switching brands of testosterone replacement gel therapy. Specifically, total testosterone levels increased significantly in patients who switched to Auxilium's Testim 1% (testosterone gel) following sub-optimal response to Androgel 1% (testosterone gel, Solvay SA).

- **BioLineRx Ltd.**, of Jerusalem, reported Phase I data at the American Psychiatric Association meeting in San Diego showing that BL-1020 was well tolerated and demonstrated biochemical evidence of dopamine blockade which is indicative of efficacy. A Phase II trial of the GABA-enhanced antipsychotic for schizophrenia is expected to begin at the end of next month.

- **Celgene Corp.**, of Summit, N.J., reported Phase II data showing that CC-10004 (apremilast) achieved the primary endpoint after 12 weeks of treatment, with 24 percent of patients receiving the oral TNF antagonist twice daily achieving a score of 75 on the Psoriasis Area and Severity Index (PASI) compared to 10 percent of those on placebo. In addition, 57 percent of CC-10004 patients achieved a PASI-50 compared to 23 percent of placebo patients, and CC-10004 patients continued to improve over time. The company said it plans to advance the product's development across a broad range of inflammatory diseases.

Financings Roundup

Continued from page 1

founded in 2000, went public in September 2005, raising about \$60.2 million in an IPO at \$12 per share. (See *BioWorld Today*, July 19, 2005, and Sept. 30, 2005.)

The Oncotype DX test uses quantitative genomic analysis in standard tumor pathology specimens to provide tumor-specific information, or the oncoprotein, of a tumor, to improve cancer treatment decisions. The clinical laboratory service entails analyzing the expression levels of 21 genes in tumor tissue samples, which generates a recurrence score based on the tumor's aggressiveness, a score believed to be correlated with the likelihood of chemotherapy benefit. The test costs \$3,460.

Genomic Health is conducting clinical studies in an attempt to expand the clinical utility of Oncotype DX in breast cancer, and is developing the product for similar diagnoses in patients with early stages of colon, prostate, renal cell and lung cancers and melanoma.

In the first three months of this year, more than 5,450 tests were delivered for use in treatment planning, compared to more than 2,900 for the year-earlier quarter. The company in its prospectus said factors that would drive broader adoption of Oncotype DX are acceptance by health care providers of its clinical benefits, demonstration of cost effectiveness, expanded reimbursement by third-party payers, expansion of its sales force, increased marketing efforts and the establishment of industry guidelines for its use.

The product's initial launch was for use in early stage, node-negative, estrogen receptor-positive breast cancer patients who will be treated with tamoxifen.

One study, to be reported at the upcoming American Society of Clinical Oncology meeting, was completed in node-positive breast cancer. Data support further investigation for prediction of recurrence, Genomic Health said. It also plans a second study focused on identifying patients more likely to benefit from anthracycline-based chemotherapy regimens. If successful, the company said, the studies could support launch for the expanded use in those patients in 2008.

Other studies are testing the utility of gene scores, the use of the product in other patient populations and use with different chemotherapy classes.

Genomic Health also is developing a second-generation product with additional genes and gene combinations, designed to increase Oncotype DX's predictive power.

The company said its strategy is to identify treatment decisions that can benefit from, and be guided by, the patient's individual genomic information. A goal is to make its genomic-based tests a standard of care, delivering information after diagnosis but prior to the decision to undergo a specific cancer treatment. It said treatment decisions now are being made with little understanding of the molecular profile of each tumor, resulting in economic inefficiencies.

Genomic Health expanded its sales team in the first quarter to 50 representatives, and said it is in the process of expanding further, with a goal of 60 representatives by

the end of this quarter.

Genomic Health said it already has reimbursement contracts with several national payers, including United Health-Care Insurance Co., Aetna Inc., Kaiser Foundation Health Plan Inc. and Cigna HealthCare. It estimated up to 20 percent of future test volume would come from Medicare patients.

Genomic Health had revenues of \$14.1 million in the first quarter, with \$13.1 million of it coming from sales of Oncotype DX (vs. \$5.1 million and \$4.2 million, respectively, for the first quarter of 2006). Its first-quarter loss was \$6.85 million. The company earlier provided full-year revenue guidance of \$57 million to \$63 million. Full-year losses were projected at \$27 million to \$30 million.

Genomic Health on March 31 reported cash and equivalents of \$35.1 million. Following the offering, it had about 27.6 million shares outstanding, as well as options outstanding on another 3 million shares at an average exercise price of \$9.94. J.P. Morgan Securities Inc. is sole book-running manager for the offering, with Lehman Brothers Inc. the co-lead manager. Piper Jaffray & Co. and JMP Securities LLC are co-managers.

In other financing news:

- **Pluristem Life Systems Inc.**, of New York, said it closed on a private investment of about \$13.5 million, a continuation of an investment announced in February. Funds will be used for its lead product, PLX-1, an allogeneic stem cell product being developed as alternative to bone marrow transplantation, and to explore the use of placental expanded mesenchymal stem cells for other indications. Separately, Pluristem purchased patents for its stem cell production technology from the Technion-Israel Institute of Technology and the Weizmann Institute of Science for about \$2 million. That deal replaces a previous license agreement in which Pluristem gained rights to the technology in exchange for a royalty rate of up to 25 percent.

- **Modigene Inc.**, of Vienna, Va., completed the second and final closing of a private placement disclosed last week, bringing total gross proceeds in the placement to about \$13 million, and \$15 million overall. An additional \$3.37 million in the private placement was provided by company officials, who also participated in the first part of the deal. Terms were the same as in the first closing. Modigene is developing long-acting versions of approved therapeutic proteins. (See *BioWorld Today*, May 16, 2007.)

- **BioMS Medical Corp.**, of Edmonton, Alberta, said underwriters from a recent financing exercised their option to purchase an additional 2.1 million units at C\$2.75 per unit. The financing now totals 16.1 million units and gross proceeds of C\$44.3 million (US\$40.8 million). Each unit consists of one common share and one-half of one warrant. Each three-year whole warrant would entitle the holder to purchase one common share at C\$4. Funds will be used to expand its clinical trial programs in multiple sclerosis and for other corporate purposes. BioMS' lead product, MBP8298, is being evaluated in two pivotal Phase III trials for secondary progressive MS patients. ■

Alzheimer's

Continued from page 1

In a paper to be published in the May 29, 2007 issue of the *Proceedings of the National Academy of Sciences*, and now available online, scientists link alterations in the wnt signaling pathway to the risk of developing late-onset Alzheimer's disease.

A previous genome-wide association study had shown a region related to Alzheimer's risk on chromosome 12. In the new paper, the researchers identified a specific single-nucleotide polymorphism that led to an amino acid substitution in a receptor for the protein wnt, and increased the risk of developing Alzheimer's in its carriers. On a cellular level, the altered wnt receptor was less active than its counterparts.

First author Giancarlo De Ferrari Valentini told *BioWorld Today* that one way Alzheimer's disease could be understood is "as a loss of function of the wnt signaling cascade. That would mean that the pathological hallmarks of AD . . . would be related to the loss of proper function of the wnt signaling cascade." Senior author Randall Moon added that the *PNAS* data showed that "patients may benefit from a weak activation of the wnt/beta-catenin pathway."

Wnt is an important developmental signaling molecule, and has been linked to several other conditions besides Alzheimer's. In fact, for Moon, the *PNAS* paper comes a mere three days after a paper in the May 19, 2007 issue of *Science* demonstrating that some forms of kidney cancer may result from abnormalities in the wnt signaling pathway.

Asked whether wnt's involvement in other diseases, especially in cancer, could prove a problem for targeting the molecule in Alzheimer's disease, Moon told *BioWorld Today* that targeting the wnt pathway sufficiently far upstream would make all the difference. The wnt pathway regulates the protein beta catenin, which regulates the steady-state level of the protein beta-catenin. Beta-catenin usually is degraded rapidly; only if the wnt pathway is activated does it accumulate.

Among its many talents, beta-catenin contributes to bone formation, and epidemiological data showed that people whose wnt pathway is unusually active have high bone density without having a higher cancer risk than normal. Moon said that shows "beyond the shadow of a doubt, that you can activate the wnt signaling pathway without causing cancer," as long as it happens upstream of beta-catenin degradation.

Because the wnt pathway influences the processing of amyloid beta, any therapeutics aimed at wnt or beta-catenin most likely would have their effects via altering amyloid beta processing. In another recent paper, published in the May 4, 2007 issue of *Science*, researchers showed that another protein also could be a promising target. By reducing levels of the protein tau, they pre-

vented the neurological deficits related to Alzheimer's disease.

In addition to amyloid plaques, tau protein aggregates – technically, neurofibrillary tangles – are a second hallmark of Alzheimer's disease. But therapeutically, tau has received less attention than A-beta. One main reason is that it has been hard to target mutant tau protein specifically.

The *Science* paper gets around that problem in the simplest of ways – by ignoring it. The researchers lowered overall tau levels with no regard to whether their tau was mutant or not.

The researchers knocked out tau in a transgenic mouse model of Alzheimer's that is engineered to express high levels of human amyloid precursor protein. Knocking out tau did not alter the high levels of amyloid-beta in the APP transgenics, but it did prevent the cognitive impairments that usually beset them.

The exact mechanism by which tau reduction could protect the brain suggested that the findings may not be limited to Alzheimer's: tau reduction protects brain cells against overstimulation. Such overstimulation contributes to a variety of neurological diseases; in their paper, the scientists showed that mice with reduced levels of tau were also resistant against epileptic seizures. ■

CLINIC ROUNDUP

- **Cougar Biotechnology Inc.**, of Los Angeles, said Phase I/II data reported at the American Urological Association meeting in Anaheim, Calif., show that 60 percent of patients treated with CB7630 (abiraterone acetate) experienced a confirmed decline in prostate specific antigen (PSA) levels of greater than 50 percent, with a third experiencing PSA declines of greater than 90 percent. Also, 20 percent more experienced a decline in PSA that was less than 50 percent. Of 20 evaluable patients with measurable tumor lesions, treatment with CB7630 resulted in partial radiological responses in 11, with seven demonstrating ongoing stable disease and three experienced regressing bone disease.

- **Cytogen Corp.**, of Princeton, N.J., reported outcomes data from a large cohort study at the American Urological Association meeting in Anaheim, Calif., demonstrating the value of the imaging product Proscint (capromab pentetide) in predicting prognosis in prostate cancer. Prostate cancer-specific death rates were 10 times higher in patients with central abdominal uptake, a finding suggestive of metastatic disease, compared to those without central abdominal uptake ($p=0.005$), further reinforcing that Proscint offers a level of accuracy and detail to prostate cancer imaging that can aid clinicians in defining patients' prognoses and treatment regimens.

Orexigen

Continued from page 1

The company's approach involves managing obesity through the central nervous system, specifically through sites in the hypothalamus that regulate appetite and energy use, while simultaneously avoiding unintended consequences. Failing to account for compensatory pathways when hitting one point in the brain's circuitry can spell doom, Tollefson explained, offsetting initial weight loss benefits by causing plateaus between 12 weeks and 16 weeks after treatment begins.

Contrave has been developed to overcome such a pitfall in the way its ingredients act to not only initiate weight loss but also sustain it. Bupropion, which is approved for depression and smoking cessation, stimulates neurons to reduce appetite and increase energy use. Naltrexone, which is approved for opioid addiction and alcohol addiction, prevents endogenous opioids from turning off the same neurons bupropion is stimulating through a natural feedback loop.

Tollefson said such a dual effect would lead "to a long, progressive reduction in weight," and do so safely, given the ingredients' long-known side-effect profiles and improvements in their formulations made by Orexigen.

He told *BioWorld Today* that the company expects to file for Contrave's approval in the second half of 2009. The registration program is evaluating a variety of obesity-related outcome measures, with the percent of weight loss from baseline to one year the four studies' primary end-point plus secondary measures related to the metabolic cascade such as blood pressure and blood lipids, and behavioral aspects associated with obesity.

That newest Phase III trial will take 56 weeks to assess Contrave's safety and efficacy compared to placebo in a comorbidity setting of about 525 obese Type II diabetics. They are being enrolled at 40 sites around the country to evaluate both weight loss as well as several factors related to glucose metabolism such as insulin sensitivity, blood sugar and hemoglobin A1c levels.

The first Phase III study of Contrave, which began in April, is looking at its weight loss potential alone or when combined with intense diet, exercise and behavior modification, compared to placebo, over the course of a year's treatment. About 800 subjects are being enrolled.

The third study, which has yet to begin, would seek to examine multiple Contrave doses against placebo to measure weight loss and impact on behaviors like mood and food cravings. Tollefson said the company has determined that a twice-daily tablet of 360 mg bupropion and 32 mg naltrexone is Contrave's optimal dose, but would like an alternative strength available to account for patient variability. A fourth study would seek to identify new dosing strategies in nonresponders and patients in whom benefits taper off to improve weight loss and keep it off.

In a previous Phase IIb trial, Contrave demonstrated statistically significant weight loss after 48 weeks of treat-

ment compared to sustained-release bupropion, immediate-release naltrexone alone and placebo.

Further development efforts at Orexigen also are targeted at obesity, namely a Phase IIb product called Empatic. Formerly known as Excalia, it combines sustained-release bupropion and sustained-release zonisamide, a drug approved for treating epilepsy that inhibits certain neurons from increasing appetite and conserving energy.

According to the Centers for Disease Control and Prevention, about a third of Americans are obese and another third are classified as overweight, and both categories are growing. There is an association between obesity and increased risk of cardiovascular disease, diabetes, orthopedic problems, breathing issues and sleep loss, among others.

"There's a litany cascade of secondary medical complications," Tollefson said, and an accompanying "intense" interest in developing optimal solutions.

Multiple pharmaceutical options are marketed for weight loss, including versions of the lipase inhibitor orlistat sold as Xenical by Basel, Switzerland-based F. Hoffmann-La Roche Ltd. and Alli by London-based GlaxoSmithKline plc, as well as Abbott Park, Ill.-based Abbott Laboratories' monoamine re-uptake inhibitor Meridia (sibutramine). Paris-based Sanofi-Aventis Group's Acomplia (rimonabant) is under FDA review, and certainly countless others remain in various stages of development.

But Tollefson does not regard the market as overcrowded, given the belief that existing drugs leave patients underserved. He said they want better options, adding that the market "clearly can handle more than one therapeutic option." And given the heterogenous nature of obesity, "there's not going to be a silver bullet" singular approach to treating everyone.

Orexigen, which has all rights to Contrave and Empatic, might consider partnering the products down the road, but Tollefson said the company would "keep our options open as long as we can."

The company sold 7 million shares at \$12 apiece in its IPO, and as of Tuesday, its stock (NASDAQ:OREX) continued to trade above that benchmark, tacking on \$2.13 to close at \$18.10. ■

CLINIC ROUNDUP

• **Enzo Biochem Inc.**, of New York, said interim data from two ongoing double-blind, placebo-controlled Phase II studies of Alequel suggested the approach induced clinical remissions and improved patients' quality of life compared to placebo. Alequel is an individualized oral immune regulation preparation consisting of an autologous protein-containing extract, individually prepared from mucosal tissue colon biopsies of the subject. The studies in 49 patients showed rates of remission and response nearly doubled in Alequel-treated patients. Enzo is enrolling additional patients in the trials.

CLINIC ROUNDUP

• **Inovio Biomedical Corp.**, of San Diego, announced that the first data from clinical trials of a DNA vaccine delivered using Inovio's electroporation approach were presented at the 3rd International Conference on DNA Vaccines in Malaga, Spain. Interim data from the Phase I/II prostate cancer study indicated that Inovio's electroporation delivery system was safe and well tolerated. Additionally, nine of 10 patients receiving the vaccine plus electroporation delivery achieved significant antibody responses compared to four of 10 patients receiving vaccine alone. The electroporation approach also is being studied in late-stage trials to improve delivery of cancer drugs. (See *BioWorld Today*, May 17, 2007.)

• **Limerick NeuroSciences Inc.**, of South San Francisco, initiated its first company-sponsored, Phase I clinical trial of LNS 5310, its lead candidate based on a strategy of chemically modulating the bioavailability of existing drugs to reduce their neurotoxicity. A physician-sponsored, proof-of-concept study was completed late last year with LNS 5662, a flavonol Pgp-modulator designed to minimize the side effects such as nausea and vomiting associated with the pain drug oxycodone.

• **NanoBio Corp.**, of Ann Arbor, Mich., reported positive Phase I safety data on NB-002 for onychomycosis, a chronic persistent fungal infection of the nail bed. There were no drug-related adverse events, serious adverse events or discontinuations due to adverse events in any of the subjects treated. In addition, plasma drug levels were below the 1 ng/mL limit of detection at all time points. The product now is in Phase II.

• **PDL BioPharma Inc.**, of Fremont, Calif., said long-term follow up data from Phase I and Phase I/II trials demonstrated that treatment with humanized monoclonal antibody Nuvion (visilizumab) on day 1 and day 2 was adequately tolerated and resulted in a sustained clinical response for up to 310 days in patients with intravenous steroid-refractory ulcerative colitis (IVSR-UC). The data, along with data indicating the potential of Nuvion in Crohn's disease, were presented at the Digestive Disease Week meeting in Washington. Nuvion is in Phase II/III for IVSR-UC and Phase II for Crohn's disease.

• **Protherics plc**, of London, said Phase IIa data reported at the Digestive Disease Week meeting in Washington showed that OncoGel improved dysphagia symptoms in nine oesophageal cancer patients. The symptoms remained unchanged for two patients, and tumor volumes decreased for eight of the 11 patients. The company plans to begin Phase IIb testing of the sustained-release formulation of paclitaxel in combination with chemoradiotherapy in the second half of this year.

• **Spectrum Pharmaceuticals Inc.**, of Irvine, Calif.,

said additional data from a Phase III registrational trial reported at the American Urological Association meeting in Anaheim, Calif., demonstrated a median time to pain progression of 66.1 weeks for the satraplatin arm compared with 22.3 weeks for placebo ($p < 0.001$). Further, pain response rates were 24.2 percent for the 351-patient satraplatin arm compared with 13.8 percent for the 181-patient placebo arm ($p = 0.005$). The double-blind, randomized, placebo-controlled study is evaluating satraplatin plus prednisone vs. placebo plus prednisone in 950 patients with hormone-refractory prostate cancer who have failed prior chemotherapy. Satraplatin is under priority review by the FDA, with an advisory committee review scheduled for July 24 and an action date set for Aug. 15.

• **Topigen Pharmaceuticals Inc.**, of Montreal, reviewed data from a Phase II study of asthma drug TPI ASM8 at the American Thoracic Society Annual Meeting in Miami Beach, Fla. In the Phase II trial, the inhaled RNA-targeted drug demonstrated significant inhibitory effects on allergen-induced responses, inhibited the influx of eosinophil cells by nearly half, and halted the increase in total cells and neutrophils after an allergen challenge. Topigen is now conducting an expanded Phase II trial with TPI ASM8.

NOW AVAILABLE:

THE BIOWORLD BIOTECHNOLOGY STATE OF THE INDUSTRY REPORT 2007

Tap into 400 pages of proprietary market research that reveals critical data and financial information about trends affecting the biotechnology industry in the U.S.

No other resource offers such a comprehensive review of the industry.

Available in print and PDF.

Call 1-800-688-2421
or 1-404-262-5476 to order!

OTHER NEWS TO NOTE

• **Acorda Therapeutics Inc.**, of Hawthorne, N.Y., reached agreement with the FDA on a special protocol assessment for a second Phase III trial of Fampridine-SR in multiple sclerosis. The primary objective of the study is to show consistent improvements in walking for drug-treated patients. The design of MS-F204 is similar to Acorda's first Phase III trial of Fampridine-SR in MS, the successful MS-F203 study. However, the current study protocol will require 14 weeks of patient participation compared to 21 weeks in MS-F203. The FDA agreed the two trials would be adequate to support a new drug application filing. The new study is being planned. Fampridine-SR is a sustained-release tablet formulation of the investigational drug fampridine (4-aminopyridine, or 4-AP), which is believed to improve communication between damaged nerves and increase neurological function.

• **Advancis Pharmaceutical Corp.**, of Germantown, Md., said the FDA accepted for filing its new drug application for Amoxicillin Pulsys for the treatment of adolescents and adults with acute pharyngitis/tonsillitis via the 505(b)(2) regulatory pathway. The company resubmitted the NDA in March after the agency rejected the first filing because it failed to include a proposed commercial batch record or a detailed commercial process description. The FDA set a PDUFA date of Jan. 23, 2008, to determine approval of Amoxicillin Pulsys, a once-a-day presentation of amoxicillin intended to offer a more convenient alternative to existing penicillin and amoxicillin regimens for patients with strep throat. Upon approval, Advancis anticipates launching the product as early as the start of the 2008/2009 cough and cold season. Shares of Advancis (NASDAQ:AVNC) gained 37 cents, or 13.6 percent, to close at \$3.10.

• **Axxam SpA**, of Milan, Italy, and **PerkinElmer Inc.**, of Boston, entered a deal under which PE will become the exclusive provider of Axxam's Photina photoprotein technology to the drug discovery market. The technology is a luminescent cell-based assay platform optimized for screening drug discovery targets, including G protein-coupled receptors and ion channels. Terms also provide for a formal research and development program for additional Photina GPCR and ion channel cell lines for use in high-throughput screening and compound profiling. Axxam retains rights to use the technology for its discovery services to third parties. Terms of the deal were not disclosed.

• **Dyadic International Inc.**, of Jupiter, Fla., said it is abandoning its Asian operations following a number of alleged improprieties that came to light after the death of the managing director for the Asian subsidiaries. Dyadic is conducting an investigation into those allegations and

has, thus far, discovered that the Asian subsidiaries' largest customer secretly was controlled by the Asian subsidiaries' management. That customer, which represented about 25 percent of the Asian subsidiaries' reported \$6.1 million 2006 net sales and about 33 percent of their \$1.7 million in net accounts receivable as of December 31, reportedly purchased products from the Asian subsidiaries which it subsequently re-sold on a cash basis to businesses in mainland China, apparently allowing the businesses to avoid Chinese reporting and sales tax requirements. Dyadic is working with the public accounting firm Ernst & Young LLP to determine proper accounting treatment to abandon those operations. As of Dec. 31, the Asian subsidiaries' assets totaled about \$4.7 million.

• **Dyax Corp.**, of Cambridge, Mass., said partner **Trubion Pharmaceuticals Inc.**, of Seattle, opted to expand its existing research agreement, which covers protein therapeutics and diagnostics discovery. In addition to the ongoing multiple-target funded research project, Dyax will transfer its phage library to Trubion's facility for use in identifying therapeutic leads to additional targets, further enabling Trubion's ability to design and develop candidates against a range of disease targets. Financial terms were not disclosed.

• **EpiStem plc**, of Manchester, UK, entered feasibility studies with London-based **AstraZeneca plc** to use its plucked hair biomarker technology to help guide preclinical and clinical development of cancer drugs. EpiStem's biomarker technology is designed to enable the measurement of effects of cancer treatments over time in a minimally invasive manner and might help inform the early stage assessment of drugs in preclinical development to reduce the risk of expensive drug failures in later clinical trials. The biomarker program evolved from EpiStem's discovery of the link between the stem cells in the small intestine and the hair follicle. Terms of the deal were not disclosed.

• **GangaGen Life Sciences Inc.**, of Ottawa, Canada, and the University of Nottingham in Nottingham, UK, agreed to engage in a research project aimed at developing a bacteriophage-based treatment for the control of *Campylobacter* bacteria in poultry. Work is expected to complement GangaGen's food safety product portfolio, which also includes phage products against *Salmonella* and *E. coli O157:H7*. Terms of the agreement were not disclosed.

• **Genome Canada, Genome Quebec** and the Université de Montréal said the Canadian government is providing C\$34.5 million (US\$31.8 million) in funding for an international consortium known as the Public Population Project in Genomics, or P3G. Counting all contributions to the program, the total budget could reach C\$64.5 million. P3G is a Montreal-based nonprofit consortium founded in 2003 that attempts to foster collaboration between researchers and projects in the field of population genomics.

OTHER NEWS TO NOTE

• **Genzyme Corp.**, of Cambridge, Mass., said a study demonstrated that administering gene therapy both systemically and directly into the brain helped to preserve motor and cognitive functions and significantly extend the lifespan in a mouse model of Niemann-Pick disease. The study tested the combination of brain and systemic injections of adeno-associated viral vectors encoding human acid sphingomyelinase, the enzyme that is deficient in Niemann-Pick disease patients. After 54 weeks of observations, Genzyme researchers found that combination therapy led to a preservation of motor and cognitive functions at near normal levels. Data were published in *The Proceedings of the National Academy of Sciences*.

• **Javelin Pharmaceuticals Inc.**, of Cambridge, Mass., signed a commercial supply agreement with **Baxter Healthcare Corp.**, of Deerfield, Ill., to provide additional manufacturing capacity for Javelin's injectable diclofenac, Dyloject, which will supplement its existing supply and manufacturing agreement. During the three-year, renewable term agreement, Baxter will serve as a secondary manufacturer of Dyloject pending regulatory approval. The agreement sets forth minimum purchase and production requirements. Financial terms were not disclosed. Dyloject is pending marketing approval in the UK and is in Phase III trials in the U.S. in acute moderate to severe pain.

• **Lpath Inc.**, of San Diego, presented proof-of-concept data from Sphingomab in an animal model of human age-related macular degeneration. Sphingomab (in its humanized form) was shown to mitigate almost completely the choroidal neovascularization formation in mice with laser-induced choroidal damage, which mimics the pathologic neovascularization experienced by patients with AMD. Sphingomab, generated by Lpath's ImmuneY2 platform technology, is a monoclonal antibody against the bioactive lipid SIP (sphingosine-1-phosphate). Lpath plans to initiate clinical trials for wet AMD in early 2008.

• **Lux Biosciences Inc.**, of Jersey City, N.J., expanded its existing technology licensing agreement with Rutgers University to add exclusive access for ophthalmic use to some of the university's polycarbonate intellectual property estate. That adds to the polyarylate patent portfolio Lux licensed from Rutgers in September 2006, and it gives

Lux access to a broader range of polymers that are bioerodible and based on long-term delivery of medications to the eye. The license includes several patents that specifically disclose methods of generating drug release formulations for peptides using polymers as the drug delivery matrix. Financial terms were not disclosed.

• **Mpex Pharmaceuticals Inc.**, of San Diego, named Daniel Burgess as CEO. He previously served as chief operating officer and chief financial officer of **Hollis-Eden Pharmaceuticals Inc.**, also of San Diego. Mpex, which discovers and develops antibacterial drugs, is in Phase I testing with its lead product, an aerosol antibiotic.

• **Pediatric Bioscience LLC**, of Sacramento, Calif., entered a deal to sponsor research at the University of California. The state will provide matching funds. The focus is to gain insight into whether certain gene expression traits are being passed on from parent to child, leading to susceptibility to autism in those children. Pediatric Bioscience was formed in 2006 by a group of researchers, parents and business people to develop products to predict, diagnose and treat children with autism.

• **Samaritan Pharmaceuticals Inc.**, of Las Vegas, signed a second exclusive marketing and distribution agreement with **Shire Human Genetic Therapies AB**, of Basingstoke, UK, to launch and sell Replagal (agalsidase alfa), a European approved drug for Fabry's disease, in Greece and Cyprus. Replagal is a long-term enzyme replacement therapy. Terms of the deal were not disclosed.

• **Synosia Therapeutics**, of South San Francisco, acquired a license from **Syngenta AG**, of Basel, Switzerland, to develop a potential treatment of Parkinson's disease. The compound, SYN-118, is a hydroxyphenylpyruvate dioxygenase inhibitor, which already is approved in the U.S. and Europe for the metabolic disorder hereditary tyrosinemia Type I. Synosia intends to develop the compound in central nervous system disorders. Under the terms, Synosia will be responsible for ongoing clinical development and commercialization of SYN-118, while Syngenta is eligible for milestones and royalties.

• **TMO Renewables Ltd.**, of Surrey, UK, licensed the ERGO bioinformatics software developed and maintained by Chicago-based Integrated Genomics Inc. for gene annotation, metabolic reconstruction and enzyme data mining, as well as for comparative genomics. The ERGO platform is expected to allow TMO to further understand and exploit its thermophilic strains to deliver green biofuels. Terms of the deal were not disclosed.

BIOWORLD PERSPECTIVES

A free, weekly e-zine offering unique viewpoints on developments within the biotech industry. Sign-up today and get a fresh outlook on topics that you can't find elsewhere!

Go to BioWorld.com and click on "Perspectives"!