BIOTECH'S MOST RESPECTED NEWS SOURCE FOR OVER 15 YEARS

BioWorld® Today

FRIDAY
MARCH 23, 2007

THE DAILY BIOTECHNOLOGY NEWSPAPER

VOLUME 18, NO. 57
PAGE 1 OF 7

Eisai Taking Over Morphotek; $325M For Antibody Foothold

By Randall Osborne
West Coast Editor

An alluring combination of platform and pipeline brought multiple would-be partners to Morphotek Inc.'s table before Eisai Co. Ltd. opted for an outright $325 million buyout. Nicholas Nicolaides, CEO of Exton, Pa.-based Morphotek, said he expects the merger to finish in four to six weeks, and Eisai, of Tokyo, plans to leave Morphotek intact as a free-standing concern, with no layoffs.

"When we got involved in the Series C financing [in 2004], we had already started to make the transition to develop our therapeutic antibody pipeline," Nicolaides told *BioWorld Today*. "It was clear in that era that there was not going to be a whole lot of value in the services business that we founded the company on, in 2000." (See *BioWorld Today*, Feb. 19, 2004.)

See Eisai, Page 2

Cubist Signs Merck Subsidiary In $45M Deal For Cubicin In Japan

By Jennifer Boggs
Staff Writer

Filling the last remaining gap in its efforts to market Cubicin worldwide, Cubist Pharmaceuticals Inc. entered a license agreement with Merck & Co. Inc. for development and commercialization of the antibiotic in Japan.

It's the seventh ex-U.S. partnership for Cubicin (daptomycin injection). The first deal dates back to 2003, when Cubist licensed rights to Chiron Corp. (now Basel, Switzerland-based Novartis AG) to develop and market Cubicin in Eastern and Western Europe, along with Australia, New Zealand, India and certain Central American, South American and Middle Eastern countries.

That deal was signed within a month of Cubicin's U.S. approval as the first lipopeptide antibiotic to treat complicated skin and skin structure infections (cSSSI) caused by

See Cubist, Page 4

Any Way You Splice It

New AMO For The Fight Against A-T And Splicing Error Diseases

By Anette Breindl
Science Editor

It's not exactly a stop-the-presses scoop that mutations in the genetic code underlie inherited diseases. But, Richard Gatti told *BioWorld Today*, "when you analyze what those mutations actually do, the focus has been very naïve until recently."

The simplest possibility (aside from a silent mutation that does nothing at all) is that a change in the DNA code leads to an amino acid substitution, which will in turn lead to a protein that is misfolded and so on, not functioning optimally.

But "there is a whole other language" beneath the classic code of DNA triplets making strings of amino acids, said Gatti, a professor of pathology at the Univer-

See Splicing Error, Page 5

NIH Initiates Phase III Trial Of Avicena's Creatine Agent for PD

By Jim Shrine
Staff Writer

The world's largest trial in Parkinson's disease got under way, testing a creatine-based neuroprotective agent from Avicena Group Inc.

The Phase III trial in more than 1,720 patients will evaluate the ability of PD-02 to slow progression in Parkinson's disease. The double-blind, placebo-controlled study, expected to take up to five years, is being run and funded by the National Institute of Neurological Disorders and Stroke of the National Institutes of Health.

The study will include patients whose disease was diagnosed no more than five years earlier and who already are on dopaminergic therapy, said Avicena CEO Belinda Tsao-Nivaggioli. Disease status will be measured by results on the Unified Parkinson's Disease Rating Scale.

See Avicena, Page 6

AHC Media LLC

Eisai

Continued from page 1

At the start of 2006, Morphotek divested its cell line evolution service business to Invitrogen Corp., of Carlsbad, Calif., keeping rights to the human Morphodoma antibody technology platform and rights to use its basic evolution platform technologies.

One of the few firms that can make fully human monoclonal antibodies in cell culture, Morphotek boasts a pair of clinical-stage drug candidates as well: MORAb 003, in Phase I/II trials for ovarian cancer, and MORAb 009, in Phase I trials for pancreatic cancer.

Nicolaides said Phase III trials with the lead candidate could begin as early as next year, but talks with Eisai will determine the course.

"As a venture-backed company, you don't have the leisure of doing multiple Phase II studies and looking at what the various pathways are," he pointed out, adding that more Phase II studies might be conducted under Morphotek's new owner.

Chris Christofferson of Menlo Park, Calif.-based Morgenthaler Ventures, which came aboard for the $26 million Series C round, told *BioWorld Today* that Morphotek's twin appeal "began to get the attention of big pharma and big biotechs pretty quickly. Morphotek fully owned all the assets and hadn't partnered any of them, so we turned Nick loose."

Some suitors were interested in the compounds and some in the platform.

"One company was only interested in the late-stage product," Christofferson recalled. "They were looking for short-term revenue potential, and there aren't many Phase II products around these days. Along came Eisai, and they said they were trying to establish long-term beachheads for worldwide development of antibodies."

Philip Sass, Morphotek's chief operating officer, said the firm knew early on that the technology applied to a wide variety of cell lines. The ability to immunize B cells in vitro and end up with fully human antibodies allowed Morphotek to "not worry too much" about others' intellectual property, such as South San Francisco-based Genentech Inc.'s recently troubled Cabilly patent.

In February, the U.S. Patent and Trademark Office invalidated the patent, which entitled Genentech to royalties – less than 3 cents of the firm's 2006 earnings per share of $2.16 – from sales of strong-selling products such as Synagis (palivizumab, MedImmune Inc.), Remicade (infliximab, Johnson & Johnson), Erbitux (cetuximab, Bristol-Myers Squibb Co.) and Humira (adalimumab, Abbott Laboratories).

Genentech is expected to appeal the patent ruling. But Morphotek need not concern itself with the outcome, thanks to solid research backing by leading academic researchers over the years. "Without them, we really wouldn't have hit this critical target," said Luigi Grasso, vice president of research and development for Morphotek.

Eisai's entry into the oncology space began with its $205 million acquisition of three cancer compounds from Ligand Pharmaceuticals Inc., of San Diego, last fall. The deal involved the marketed products Ontak (denileukin diftitox), for cutaneous T-cell lymphoma; Targretin (bexarotene) gel and capsules, also for CTCL; and Panretin (alitretinoin) gel for Kaposi's sarcoma, an AIDS-related skin cancer.

Cathy Pollini, spokeswoman for Eisai, told *BioWorld Today* that the strategy in acquiring Morphotek "is to look at complementing the small-molecule efforts we have in place, and potentially do a combination of the two."

Christofferson said he was pleased to see the trend exemplified by Eisai's Morphotek buyout, as the much talked-about industry consolidation goes on.

"What's happened is different than people thought," he said, adding that many, when they spoke of consolidation, meant biotech-biotech mergers. "People sort of ignored the possibility that this process could be big [pharma] companies buying the biotechs," he said.

Investors played a major role in shaping Morphotek, Christofferson said, and the decision to develop the pipeline made possible a deal that likely would not have happened if the firm had stuck with its platform alone.

"You've got to have products," he said. ■

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. (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

Topigen, Novagali Partner For Technology Swap Collaboration

By Trista Morrison
Staff Writer

Although Topigen Pharmaceuticals Inc. and Novagali Pharma SA may not appear at first to have much in common, the two companies swapped technologies through a strategic collaboration and cross-licensing agreement.

Terms of the deal were not disclosed, but Topigen President and CEO Paul Wotton said the agreement involves a "sharing of technologies" in which Topigen will provide access to its RNA targeting platform while Novagali will provide a license to its topical drug delivery formulation. The deal allows both privately held companies to leverage their strengths while expanding into a new area.

Financial considerations will not come into play until further "down the road," Wotton said, adding that such an arrangement could likely "only happen between two biotechs."

Montreal-based Topigen is developing a pipeline of inhaled small molecules and RNA-targeted oligonucleotides for respiratory diseases. The company's lead compounds are TPI ASM8, a Phase II inhaled RNA-targeted asthma drug, and TPI1020, a Phase II inhaled nitric-oxide formulation of budesonide licensed from NicOx SA for use in treating chronic obstructive pulmonary disease. Topigen also is developing earlier-stage programs in COPD and allergic rhinitis. (See *BioWorld Today*, Oct. 28, 2005.)

The agreement with Novagali provides Topigen with an exclusive license to use Novagali's Novasorb topical delivery technology in the development of an RNA-targeted drug for allergic rhinitis.

Topigen already is conducting preclinical studies with TPI ALR8, a derivative of asthma drug TPI ASM8. Both drugs are chemically modified antisense oligonucleotides designed to affect multiple inflammatory cytokine receptors, creating a synergy between pathways that would allow for low-dose treatment.

While TPI ASM8 is inhaled to the lungs, TPI ALR8 will be delivered intranasally, which is where Novagali's Novasorb topical delivery technology comes into play. "We believe [the Novasorb technology] would improve uptake of the drug into the nasal membrane," Wotton said.

Novasorb is a cationic emulsion designed to improve retention time for drugs delivered via tissues such as the cornea and conjunctiva. Although it has not been tested in human nasal membranes, Wotton said the approach is "very appropriate" for developing a product that's "efficacious and easy on the nose."

The Novasorb technology has served as the backbone for Evry, France-based Novagali's pipeline of ophthalmic specialty pharmaceuticals. Chief among them are Cationorm, an OTC dry-eye drug, and Nova22007, a Phase III severe chronic allergic conjunctivitis treatment. Novagali's pipeline includes several other treatments for conditions of the anterior and posterior segment of the eye, including a glaucoma drug.

In exchange for licensing Novasorb to Topigen, Novagali gets an exclusive worldwide license to use Topigen's RNA-targeting platform technology to develop an ophthalmic product to treat and prevent allergic eye diseases. These diseases are mediated by many of the same chemokines and cytokines involved in asthma, where Topigen's RNA-targeting approach already has generated positive data in initial Phase II trials.

The two companies plan to form a collaborative committee to advise each other on the development of both the ocular and nasal Novasorb RNA-targeted products. If all goes well, the intranasal formulation for allergic rhinitis will enter the clinic in 18 to 24 months. ■

OTHER NEWS TO NOTE

• **Aegerion Pharmaceuticals Inc.**, of Bridgewater, N.J., said in its S1 filing that it entered into a $15 million loan and security agreement with Hercules Technology Growth Capital Inc. Aegerion has borrowed $10 million thus far, and the company expects to use proceeds from its initial public offering in part to repay the outstanding amount. (See *BioWorld Today*, March 22, 2007.)

• **Alfacell Corp.**, of Bloomfield, N.J., said in vitro studies show that mild hyperthermia enhances the therapeutic effects of its lead candidate, Onconase (ranpirnase). Data show that apoptosis increased up to 200 percent when Onconase was applied to lymphoblastoid TK6 cells at 40 degrees Celsius (104 degrees Fahrenheit) compared to treatment at 37.5 degrees Celsius. In those experiments, apoptosis was manifested by classical changes in cell morphology and the activation of caspase-3. Results were published in the *International Journal of Oncology*.

• **Alnylam Pharmaceuticals Inc.**, of Cambridge, Mass., and Stanford University published a study in the journal *Cell* on the role of microRNAs in immunity. In the preclinical study, a specific miRNA, miR-181a, was shown to play an important role in controlling T-cell responsiveness to antigens by regulating the T-cell-receptor signaling pathway. Alnylam said the findings further validate miRNAs as disease targets and point to new potential therapeutic applications for antagomirs, a class of oligonucleotide-based inhibitors of specific miRNAs.

• **Cobalis Corp.**, of Irvine, Calif., received $675,000 in the third and final closing of its previously announced private placement of 8 percent senior secured convertible debentures. The third close brings the total raised to $3.85 million, including a December first-close of $2.5 million and a February second-close of $675,000. Proceeds will be used to complete data analysis of the company's two completed pivotal Phase III allergy trials with PreHistin, data from which are expected in April.

Cubist

Continued from page 1

Gram-positive bacteria.

"We've worked with various partners during the life of" Cubicin's development, said Eileen McIntyre, senior director of corporate communications for Lexington, Ky.-based Cubist. "We entered agreements that reflected the opportunities at that time."

Through the most recent deal, the company adds an established Japanese firm as its partner: Tokyo-based Banyu Pharmaceutical Co. Ltd., a wholly owned subsidiary of Whitehouse Station, N.J.-based Merck, which previously achieved commercialization in Japan of Tienam, a carbapenen antibiotic.

In exchange for Cubicin rights, Merck will make an upfront cash payment of $6 million to Cubist, plus up to $39.5 million in regulatory and sales milestones. Merck also agreed to pay an undisclosed transfer payment that would include the cost of producing Cubicin, as well as an amount to cover Cubist's royalty payment to Indianapolis-based Eli Lilly & Co., which originally developed the product, and a margin to Cubist, McIntyre said.

Under its license, Merck, through Banyu, will seek approval of Cubicin in cSSSI and bloodstream infections. Though Merck has not disclosed a timeline for Japanese approval of Cubicin, it said that Banyu "does expect to conduct some additional, Japanese-specific studies" prior to regulatory filing, McIntyre told *BioWorld Today*.

A once-daily intravenous product, Cubicin is approved in the U.S. for cSSSI, including strains of methicillin-resistant *Staphylococcus aureus* (MRSA), and for bacteremia, including right-sided infective endocarditis caused by MRSA and methicillin-susceptible staph infection. Cubist markets the antibiotic itself in the U.S., and fourth-quarter sales totaled $56.4 million, marking a 54 percent increase over fourth-quarter 2005.

The company has projected peak U.S. Cubicin sales at $500 million, McIntyre said.

The product, however, might have to face some competition soon in the U.S. Gram-positive infection space. South San Francisco-based Theravance Inc. expects an FDA decision on telavancin, a once-daily injectable lipoglycopeptide, in cSSSI in the second half of this year, and Targanta Therapeutics, of Cambridge, Mass., anticipates filing a new drug application later this year for its once-daily glycopeptide antibiotic, oritavancin, in cSSSI. (See *BioWorld Today*, Dec. 11, 2006, and Feb. 12, 2007.)

Outside the U.S., Cubicin has gained approval in Europe in cSSSI and awaits a regulatory ruling on a separate application for bacteremia. The product was launched in Israel in 2004 by partner Medison Pharma Ltd, and later this year, will hit the market in Taiwan through a licensing agreement with TTY Biopharm Ltd.

"There have also been filings done in several other countries," McIntyre said, including Canada, for which partner Oryx Pharmaceuticals Inc. anticipates approval later this year, and Korea, where Cubicin also is expected to gain approval this year by partner Kuhnil Pharmaceuticals.

In December, Cubist licensed Chinese rights to London-based AstraZeneca plc in a deal calling for $10.25 million up front and undisclosed regulatory and sales milestones. McIntyre said AstraZeneca expects regulatory filing this year.

Beyond cSSSI and bacteremia, Cubist is exploring Cubicin dosage levels in a Phase II study in osteomyelitis. Since the product gets "some off-label use in that indication, the FDA thought it would be a good idea" to determine an appropriate dosage level, McIntyre said.

Cubist, which reported net income of $5.4 million, or 10 cents per share, for the fourth quarter, ended the year with a cash position of $309.2 million. The company's stock (NASDAQ:CBST) closed at $20.84 Thursday, up 44 cents. ■

OTHER NEWS TO NOTE

• **Cytyc Corp.**, of Marlborough, Mass., said it now has purchased more than 92 percent of the outstanding shares of **Adeza Biomedical Corp.**, of Sunnyvale, Calif. It previously had purchased about 87.4 percent of Adeza's shares, which had been tendered in the offering period that expired March 16. The subsequent offering period for any remaining Adeza shares will expire at midnight March 30. The same price of $24 per share offered in the initial period will be paid in the subsequent period.

• **DiaMedica Inc.**, of Winnipeg, Manitoba, said it completed a C$5.5 million (US$4.75 million) initial public offering on the TSX Venture Exchange in Canada. The company sold 5.5 million shares at C$1 each. Dundee Securities Corp. and Research Capital Corp. underwrote the offering. DiaMedica is developing products for Type II diabetes based on a mechanism involving nerve signaling to the liver. The lead product, DM-71, is in a Phase IIa trial. It also is developing two other products, DM-83 and DM-99. The stock (CDNX:DMA) closed down C10 cents Thursday at C$1.10.

• **Genetic Technologies Ltd.**, of Melbourne, Australia, entered a deal under which Tampa, Fla.-based **UTEK Corp.** will help it identify genetic analysis intellectual property developed by U.S.-based researchers that may be of interest to GTL's genetic testing business. The initial focus of the relationship will be in the area of non-coding DNA analysis. Terms were not disclosed.

• **Mymetics Corp.**, of Nyon, Switzerland, said all litigation with MFC Merchant Bank SA was resolved. The dispute related to a €4 million (US$5.3 million) credit facility provided by the bank. Mymetics agreed to pay Geneva-based MFC €1.49 million and provide 12.5 million restricted shares. All liens held by MFC on Mymetics' intellectual property were relinquished.

Splicing Error

Continued from page 1

sity of California, Los Angeles' David Geffen School of Medicine. And one of the things that language describes is how to cut the relevant bits out of the original transcript and paste them together – a process known as splicing.

"Sixty to 70 percent of all proteins are alternatively spliced," he said. In other words, "you can leave out exon 24 or you can keep it in, and that will give you a different protein," Gatti added.

When it goes according to plan, alternative splicing is a comparatively frugal way for proteins to diversify – making a protein that is either membrane-bound or soluble, for example, from the same starting DNA sequence.

But splicing can, and does, go wrong. In fact, in a paper published this week in the early online edition of the *Proceedings of the National Academy of Sciences*, Gatti and his colleagues stated that "the majority of all inherited diseases result from mutations that cause aberrant splicing." In the paper, they show that mutations leading to cutting errors underlie the genetic disorder ataxia-telangiectasia, and that using a contraption known as antisense morpholino oligonucleotides, or AMOs, to mask such mutations can restore the affected kinase in cells from ataxia-telangiectasia patients.

Ataxia-telangiectasia (A-T) is a DNA repair disease. It results from mutations in a kinase that leave cells unable to properly repair DNA and, consequently, patients with a host of problems, from increased susceptibility to cancer to neurodegeneration. Half of those afflicted do not live past their teen years.

Many different mutations can cause A-T, which, Gatti said, is not all that untypical. "There are a few diseases where one mutation causes most of the disease – cystic fibrosis is a good example," he said. "But in the case of most other genes, there are many different mutations – the BRCA gene is an example. The larger a gene is, the longer it is, the more mutations you'll see."

That variety makes research on cells from A-T patients experimentally tractable. "We have many ways of testing whether the cells function, because the A-T cells have a lot of phenotypes that can be corrected."

Gatti and his team used AMOs to correct mutations in the A-T gene that led to improper splicing. Essentially, AMOs were "put as a patch over the mutation in the pre-RNA," Gatti said. For three different splice mutations, the procedure restored proper splicing and led to kinase levels that were anywhere from 5 percent to 25 percent of normal levels. While that may not sound like much, mutation carriers often are unaffected despite having kinase levels that are only 40 percent to 50 percent of what is normal – so 100 percent restoration probably will not be necessary to achieve clinical success.

The current paper follows another paper published by the same group in 2004 showing a way to correct another type of mutations in the kinase: premature stop codons that lead to truncated proteins, which affect around 30 percent of patients. Splice-site mutations affect about half.

"Our lab is working very hard on bringing the concept of mutation-based therapy to the clinic," Gatti said. The major obstacle is not in the scientific rationale, but in a much more pedestrian area: "We have the same problem as gene therapy – we need a delivery vehicle."

The reason is that, at a cost of roughly $3,000 per gram, morpholinos for A-T patients would be extremely expensive using general delivery. In fact, it would make the $10,000 a month cost of some monoclonal antibodies look like dollar store pricing. Gatti said that according to a rough calculation of his, the cost to treat a single A-T patient with AMOs "worked out to around $5 million," and that's assuming untargeted delivery would work at all.

"It stays in the bloodstream; that's not a problem," Gatti said. "The question is how we're going to get such an expensive compound to concentrate in the organs. Once that's solved, we've shown with this paper that we know exactly how to design [AMOs] for this disease." ■

OTHER NEWS TO NOTE

• **NuWay Medical Inc.**, of Irvine, Calif., completed its corporate name change to **BioLargo Inc.**, and is trading on the Pink Sheets under a new symbol, "BLGO." The change is intended to reflect the company's mission to develop and commercialize BioLargo technology, aimed at producing iodine on demand, in controlled dosages, to be used as a disinfectant in products across multiple industry lines. The company also completed a 1-for-25 reverse stock split, and converted $2.2 million aggregate principal amount of convertible notes into an aggregate of 6.1 million shares on a post-reverse split basis.

• **ProMetic Life Sciences Inc.**, of Montreal, and **Tecpar**, of Curitiba, Brazil, have signed a technology transfer and licensing agreement allowing Tecpar to manufacture a complex biopharmaceutical product for the Brazilian domestic market as well as all other South American countries. The total transaction is valued at C$19 million (US$16.41 million). ProMetic will manage development of the manufacturing process, which is based on technology licensed from a division of the National Research Council of Canada, and ProMetic's own bioseparation process. ProMetic has granted Tecpar an exclusive license to use the technology for a selected biopharmaceutical product for the entire South American market. ProMetic will received about C$9 million for license, milestone and development payments. Also, C$10 million will go to modify Tecpar's current facility.

Avicena

Continued from page 1

PD-02 is an ultra-pure form of creatine designed to boost production of ATP, or adenosine triphosphate. The product, from Avicena's cellular energy modulation platform, targets the creatine kinase enzyme for increasing production or delivery of cellular energy. The company also is testing creatine formulations in other neurodegenerative diseases.

"We are very encouraged by the collaboration with the NIH, and very happy they are funding the Phase III trial," Tsao-Nivaggioli told *BioWorld Today*. "It is also nice to see such a good network of neurologists working on the trial," which will include more than 50 sites in the U.S. and Canada.

She said interim data are expected to be released along the way, but the timing is dependent on the rate of enrollment. The study design in earlier-stage patients was approved in April 2006 by the FDA, which first wanted the company to conduct a dose-escalating chronic toxicology trial. That study was completed in February.

Avicena is providing drugs for the Phase III trial, and will have rights to the study results, and retains complete ownership of the product, Tsao-Nivaggioli said.

Avicena was founded in the late 1980s as Amira Inc. and was acquired by Repligen Corp. in 1991. Amira's initial focus was on inhibition of the creatine kinase enzyme, or taking energy away from cells, a process that might have cell death-related oncology applications.

Avicena, spun back out of Repligen in the late 1990s, realized it might be easier to use the technology to boost cellular energy for neurodegenerative diseases, rather than inhibit it, since energy deficit was one of the common underlying themes in such diseases.

A higher-dose formulation of creatine, HD-02, is undergoing toxicology studies in preparation for a Phase III trial in Huntington's disease, which Tsao-Nivaggioli said is expected to begin late this year or early in 2008.

The company also has cellular energy regulation programs in amyotrophic lateral sclerosis. Testing of ALS-08 recently began in a Phase II trial evaluating its efficacy, safety and tolerability in separate combinations with minocycline and celecoxib. The combination with the better result will be taken into a more traditional Phase II trial, she said. A Phase III trial of another ALS compound, ALS-02, that was completed in May 2006 showed improved mortality outcomes but did not meet primary or secondary endpoints.

Tsao-Nivaggioli said Avicena is starting a dose-escalation study of ALS-02 before moving into studies to evaluate survival.

Avicena separately has a line of skin care products, a business to supply dermaceutical ingredient blends, and a creatine-based nutritional supplement program, Neotine, designed to promote neuronal cell health.

Avicena reported less than $100,000 in cash and equivalents as of Sept. 30, with nine-month revenues of about $313,000 and a nine-month loss from operations of $3.8 million. Since then it has raised at least $2.5 million in a private financing. The company is in the process of seeking additional funds, Tsao-Nivaggioli said.

Avicena had 51 million shares outstanding as of Sept. 20. Its stock (OTC BB:AVGO) closed at $5.85 Thursday, unchanged. ■

CLINIC ROUNDUP

• **Aeolus Pharmaceuticals Inc.**, of Laguna Niguel, Calif., finished analyzing results from its Phase I multiple-dose study of AEOL10150, and said the clinical direction for the drug is under consideration, with the most likely targets for an efficacy study being lung cancer and/or head and neck cancer and amyotrophic lateral sclerosis. The 18-patient trial studied three doses of AEOL10150 or placebo administered subcutaneously, and results showed that the drug was safe and well tolerated at doses up to 2 mg/kg/day. AEOL 10150 is a small-molecule catalytic antioxidant designed to protect healthy cells in radiation therapy.

• **AEterna Zentaris Inc.**, of Quebec City, and its partner, **Shionogi & Co. Ltd.**, of Osaka, Japan, reported positive results for a Phase IIa trial of cetrorelix in benign prostatic hyperplasia, showing that the drug, a luteinizing hormone-releasing hormone antagonist, was safe and well tolerated at all dosage regimens. Data from the trial, which involved about 50 Japanese patients, also showed that patients responded to cetrorelix with a transient reduction of testosterone concentration in blood, which did not reach or remain at the castration level. Based on those results, Shionogi initiated a 300-patient Phase IIb study to assess the efficacy of cetrorelix in BPH in Japanese patients.

• **Celldex Therapeutics Inc.**, of Phillipsburg, N.J., is sponsoring a Phase II trial of its vaccine for treating glioblastoma. The vaccine targets an epidermal growth factor receptor variant, or EGFRvIII. The study will enroll 81 patients whose tumors produce the altered protein. An earlier, small Phase II trial in glioblastoma showed encouraging survival results.

• **Evotec AG**, of Hamburg, Germany, initiated a Phase I study of EVT 302, a monoamine oxidase B enzyme in development for smoking cessation. The open-label study is designed to access the occupancy of the MAO-B in the brain after administration of single oral doses of the drug by the use of dynamic positron emission tomography. The company plans to start additional Phase I studies during the first half of this year, and pending successful results, will move into Phase II development in mid-2008.

OTHER NEWS TO NOTE

• **Pro-Pharmaceuticals Inc.**, of Newton, Mass., entered into definitive agreements with six of seven investors to exchange $3.9 million of their $4.4 million worth of 7 percent convertible debentures for 5.2 million shares of common stock priced at 75 cents per share. The financial restructuring retired most of the debentures that had a floorless redemption provision and reduced the exercise price of associated warrants from $3.35 to $1. The company is scheduled to meet with the FDA in April to discuss data and plans for submitting a new drug application under Section 505(b)(2) for lead drug Davanat co-administered with 5-fluorouracil in cancer.

• **Provagen**, of Greensboro, N.C., was launched as the first spin-off firm of North Carolina Agricultural and Technical State University, based on research conducted at the School of Agriculture and Environmental Sciences. Provagen plans to produce and market a protein, Protein V, that can be used in medical research or in manufacturing treatment and diagnostic tests for diseases. A&T will retain equity in the company and earn royalties on the product. Protein V has been shown to form strong chemical bonds to antibodies, which makes it possible to extract them from blood serum.

• **VASTox plc**, of Oxford, UK, has completed the simultaneous acquisition of **DanioLabs Ltd.**, a private Cambridge, UK-based drug discovery company, and **Dextra Laboratories Ltd.**, of Reading, UK, a specialist carbohydrate chemistry service company. The £16.5 million (US$22 million) in acquisitions brings to VASTox two clinical and two pre-clinical programs in neurological and ophthalmic diseases. Daniolabs was acquired for £15 million payable through the issuance of 11,732,361 new 10p ordinary shares and cash of £159,000 to DanioLabs' existing shareholders based on a VASTox share price of 126.5p, calculated as an average share price over a 10-day period ending March 20. Of those shares, 1,173,233 will be deferred and issued in one year provided no warranty claims arise. As of July 31, DanioLabs recorded net assets of £2.74 million and a loss on operating activities before taxation of £2.76 million. Dextra was purchased for £1.5 million, payable through the issuance of 1,185,771 new 10p ordinary shares to Dextra's existing shareholders. As of Sept. 30, Dextra reported net assets of £0.17 million and a profit on operating activities before taxation of £0.07 million. In December, VASTox bought the bankrupt MNL Pharma Ltd. for its library of natural imino sugars, a preclinical portfolio and a carbohydrate chemistry laboratory.

• **Vion Pharmaceuticals Inc.**, of New Haven, Conn., extended its manufacturing agreement with SAFC, a member of St. Louis-based **Sigma-Aldrich Group**, for its lead cancer drug, Cloretazine (VNP4010M) until September 2009. SAFC will continue to manufacture the product's active pharmaceutical ingredient. Financial terms were not disclosed. Cloretazine, an alkylating agent, is being tested in a Phase III trial in combination with cytarabine in relapsed acute myelogenous leukemia and in Phase II pivotal study as a single agent in elderly patients with previously untreated de novo poor-risk acute myelogenous leukemia.

CLINIC ROUNDUP

• **GPC Biotech AG**, of Martinsried, Germany, and **Spectrum Pharmaceuticals Inc.**, of Irvine, Calif., said additional data from a Phase III trial of satraplatin in refractory cancer showed that pain response rates for patients treated with satraplatin plus prednisone (24.2 percent) were statistically superior compared to the pain response rates for patients in the placebo arm (13.8 percent.) Those results were presented at the European Association of Urology Congress in Berlin. GPC and Spectrum completed a rolling new drug application last month, seeking approval of satraplatin in prostate cancer. GPC's European marketing partner, Boulder, Colo.-based **Pharmion Corp.**, plans to file for approval in Europe in the first half of this year. (See *BioWorld Today*, Feb. 20, 2007.)

• **Peregrine Pharmaceuticals Inc.**, of Tustin, Calif., completed enrollment of the planned 12 evaluable patients in its Phase Ib trial of bavituximab in combination with common chemotherapy agents in advanced cancer patients with metastatic disease who had failed prior therapy. Data from that study are expected to support the initiation of Phase II trials later this year. Bavituximab is a monoclonal antibody designed to target and bind to phosphatidylserine, which is located on the inside of normal cells but becomes exposed on the outside of cells that line the blood vessels of tumors.

• **Xanthus Pharmaceuticals Inc.**, of Cambridge, Mass., began a Phase I dose-escalation study of Clomet (DMPEN, 4-demethylpenclomedine) in patients with solid tumors. The trial is expected to enroll as many as 25 patients to receive a daily dose of Clomet for three consecutive days as a short infusion for four cycles. Primary objectives include determining the product's safety profile, identifying dose-limiting toxicity, finding the maximum tolerated dose and studying the pharmacokinetics, while secondary objectives will assess preliminary evidence of antitumor activity.