

# BIOWORLD® TODAY

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PAGE 1 OF 9

## BioMarin Stops Development Of Neutralase In CABG Surgery

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

Officials at BioMarin Inc. believe themselves to be fortunate in determining fairly early that their lead product, Neutralase, probably won't make it to market.

In response to a recommendation Friday from an independent Data Safety Monitoring Board (DSMB), BioMarin stopped its Phase IIIa study of Neutralase in coronary artery bypass graft surgery and has terminated further development of the experimental drug. Neutralase was being evaluated for the reversal of anticoagulation by heparin in primary CABG surgery.

The company's stock (NASDAQ:BMRN) on Monday closed at \$7.93, down 66 cents.

Even though Neutralase was BioMarin's No. 1 candidate with a potentially large market, Yaron Werber, a biotech-  
*See BioMarin, Page 3*

### *Financing Roundup*

## Pain Therapeutics Raises \$49.7M In Follow-On; Neose Getting \$23M

**By Brady Huggett**  
**Associate Managing Editor**

Pain Therapeutics Inc. priced its public offering of about 7.7 million shares at \$6.50 per share, raising gross proceeds of \$49.7 million.

The company filed for the offering in August. Its stock (NASDAQ:PTIE) fell 44 cents Monday to close \$6.25. (See *BioWorld Today*, Aug. 25, 2003.)

South San Francisco-based Pain Therapeutics said it plans to use the funds for general corporate purposes, including research and development projects, the development or acquisition of new products or technologies, general working capital and operating expenses. The company had expected to price the offering last week, but Hurricane Isabel forced the closing of the SEC and therefore  
*See Financing, Page 5*

### *North-South Lyme War Between States*

## Controversy Smolders As To U.S. Regions Of Lyme Disease, *Borrelia burgdorferi*, Despite M.D. Practices

**By David N. Leff**  
**Science Editor**

The bacteria that cause Lyme disease, *Borrelia burgdorferi*, are found of late in multiple rodent and tick species of the Southeastern United States. Lyme disease – an infection transmitted between ticks and many vertebrate species – is the most common parasite-borne illness in the U.S. and Europe. More than 80 percent of U.S. cases occur in the Northeastern and mid-Atlantic states.

Because few people are infected in the Southern states, notably Georgia, Florida and South Carolina, pathologists had questioned whether ticks and host species there carried the "true" causative spirochete bacteria. To settle this  
*See Lyme Disease, Page 9*

## First-Round Financing Of \$12.5M Puts Ambrx On Development Path

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

Ambrx Inc. is hitting the ground running with \$12.5 million from a Series A round of financing along with an exclusive license to its technology from the Scripps Research Institute.

The San Diego-based company also rounded out its executive team with the appointment of CEO Richard DiMarchi and Chief Scientific Officer Thomas Daniel. DiMarchi was one of Ambrx's founders, along with Peter Schultz, its chairman, and Troy Wilson, its chief business officer.

It was founded on technology developed for nearly two decades by Schultz and his colleagues at Scripps. Designed to allow for the genetic engineering of proteins with new amino-acid building blocks, beyond the common  
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**INSIDE:** GENZYME INVESTS \$37.7M IN CAT AS COMPANIES RESTRUCTURE PACT ....2  
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★

## Genzyme Invests \$37.7M In CAT As Companies Restructure Pact

By Nuala Moran

*BioWorld International* Correspondent

LONDON – Cambridge Antibody Technology Group plc and Genzyme Corp. are strengthening their ties, with CAT increasing its financial contribution to joint work on anti-TNF-beta antibodies and Genzyme investing £22.9 million (US\$37.7 million) in 4.3 million CAT shares, raising its total stake to 11 percent.

When the companies set up their collaboration in September 2000, the agreement gave CAT the right to get a greater share of any profits by putting more money into the development program. Although the amount of money was not disclosed, CAT said it now is committed to fund 50 percent of the development costs over the next two years, "significantly increasing" its share of the profits.

CAT CEO Peter Chambre told *BioWorld International*, "CAT's goals and strategy are based on investing in a number of key products in clinical development where we can get significant returns. We think the anti-TNF-beta program is potentially very high value."

He added that the equity investment from Genzyme would enable Cambridge, UK-based CAT to fully fund its share of the anti-TNF-beta program and was a sign of Genzyme's commitment to its collaboration with CAT. Under the initial deal Genzyme, of Cambridge, Mass., made a \$20 million equity investment in CAT for 307,982 shares.

The two also amended their agreement to give each other the right to purchase the other's interest in the program if either is acquired by a third party.

Chambre said the money that CAT is committing will accelerate the clinical development of antibodies against TNF-beta, which is implicated in a number of fibrotic disorders and scarring. The lead product in the collaboration, CAT 192, has completed a Phase I/II trial in the treatment of scleroderma, with initial results expected in the fourth quarter. An IND will be filed with the FDA for the second

product, GC-1008, in the treatment of idiopathic pulmonary fibrosis before the end of 2003. GC-1008 is the lead product in a series of anti-TNF-beta human monoclonal antibodies, and it is expected that trials of other products in the series will follow.

CAT already has established proof of efficacy for an anti-TNF-beta antibody in preventing scarring following surgery for the eye disease glaucoma. The product, called Trabio, recently completed enrollment in a Phase II/III European study, and CAT is looking for a partner. Trabio and the use of other anti-TGF-beta antibodies to treat ophthalmic diseases are excluded from the Genzyme/CAT collaboration.

CAT also announced a further expansion of its 1998 licensing agreement with Dyax Corp., of Cambridge Mass., granting Dyax an increased number of options for licenses to develop antibody products under CAT's phage display patents. In return, Dyax gave up the right to any royalties due from CAT on Humira, an antibody treatment for rheumatoid arthritis launched at the beginning of 2003 by CAT's partner, Abbott Laboratories.

CAT is entitled to milestones and royalties on any products Dyax develops. Chambre said the deal was a good one because it had enabled CAT to cancel royalty obligations to Dyax without paying cash, and expands its antibody licensing. "Our explicit focus is that outside the areas on which we focus, we will broadly license," Chambre said. ■

## OTHER NEWS TO NOTE

• **Agencourt Bioscience Corp.**, of Beverly, Mass., introduced QuickLane Research Sample Sequencing, a sequencing service for individual research samples. Researchers now can submit a single sample for sequencing using Agencourt's genomics pipeline and receive results within 24 to 48 hours.

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## BioMarin

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nology analyst with S.G. Cowen Securities Corp. in New York, told *BioWorld Today* Wall Street has been skeptical at best about the trial ending in success. Not only that, he said, the company has been criticized for allocating so much money to develop the drug. "In that regard, it is certainly encouraging that they caught it early and decided to terminate development earlier, rather than later."

The DSMB recommended that BioMarin stop enrollment due to an increasing frequency of adverse events observed in the Neutralase group, Joshua Grass, BioMarin's manager of investor relations, told *BioWorld Today*. The company is not prepared to release a list of the events, he said, adding, "This was late-breaking news on Friday. When we get more data, we'll be able to determine exactly what the adverse events were."

However, "the adverse events were not uncommon to those observed in CABG surgery; they were just more common in the group that was receiving Neutralase," Grass said.

Neutralase, a carbohydrate-modifying enzyme that cleaves heparin, was acquired by BioMarin in its 2001 buy-out of Montreal-based IBEX Technologies Inc. Heparin is necessary in all CABG procedures to avoid potentially fatal complications arising from blood clotting during the operations, but the drug can cause excessive bleeding after surgery and must be reversed. (See *BioWorld Today*, Oct. 1, 2002, and Oct. 11, 2001.)

In a conference call with investors, analysts and reporters Monday morning, Fredric Price, chairman and CEO of Novato, Calif.-based BioMarin, said terminating further development of Neutralase was the best decision for both the stockholders and the company. BioMarin has worldwide rights to the drug.

"Based on our top-line analysis, the problems observed with Neutralase could not be addressed by change to the clinical protocol or study design," Price said. "There were no deaths in the study related to Neutralase, but there was one death in the protamine arm, but this isn't an unusual event given the critical nature of CABG surgery."

According to the company, 150 patients out of the targeted 600 had enrolled in the study. The primary endpoint was non-inferiority of Neutralase to protamine, measured by cumulative chest tube drainage.

Neutralase failed in a previous Phase III in CABG surgery while under the ownership of IBEX. That trial was believed to have been unsuccessful due to dosing.

But in earlier Phase I/II trials, Grass said Neutralase performed well. "Earlier trial data suggested that Neutralase was effective in stopping bleeding, and it didn't show some of the adverse events that were associated with protamine, which is the current standard of care."

BioMarin in early June offered about \$125 million in convertible subordinated notes due in 2008. The company

has a healthy pipeline and was looking for funds to help support its trials. (See *BioWorld Today*, June 18, 2003.)

As of June 30, BioMarin had about \$265 million in cash and cash equivalents. On deciding to stop development of Neutralase, BioMarin revised its financial estimates. For 2003, the company reduced its forecasted net loss to \$76 million to \$78 million, down from \$81 million to \$83 million. Its cash burn rate has dropped to \$74 million to \$78 million, down from \$80 million to \$84 million.

For 2004, the company changed its forecasted net loss to \$68 million to \$70 million, down from \$81 million to \$83 million. The cash burn drops from \$69 million to \$73 million, down from \$80 million to \$84 million.

As for the good news, Werber told *BioWorld Today* that Aldurazyme, an enzyme replacement therapy for mucopolysaccharidosis-I recently launched by BioMarin and partner Genzyme General, of Cambridge, Mass., is on track to meet guidance estimates of \$10 million to \$13 million this year.

BioMarin and Genzyme received FDA approval in May for Aldurazyme. (See *BioWorld Today*, May 1, 2003.)

Elsewhere in the pipeline, BioMarin is conducting a pivotal Phase III trial evaluating Aryplase in mucopolysaccharidosis-VI, also a genetic disease.

Price told conference call listeners he expects to file a new drug application for Aryplase in September or October 2004, and if all goes well, the product could reach the market in the second or third quarter of 2005. The FDA awarded Aryplase fast-track and orphan status. Price expects to partner Aryplase outside the U.S.

The company also is conducting a Phase Ib study of Vibrilase, an enzyme candidate for the treatment of serious burns. BioMarin likely will out-license Vibrilase.

Price said BioMarin believes it will enter the clinic in 2004 with a treatment for phenylketonuria (PKU), a genetic disease affecting 50,000 children in the Western world. PKU is characterized by an inability to oxidize a metabolic product of phenylalanine and by severe mental retardation. ■

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## OTHER NEWS TO NOTE

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• **Alynham Pharmaceuticals Inc.**, of Cambridge, Mass., entered a licensing agreement with Stanford University in Palo Alto, Calif., for intellectual property related to the method for inducing gene silencing through RNA interference (RNAi) in adult mammals. More specifically, the co-exclusive therapeutic license is related to a patent application and related technology based on the research of Mark Kay, Anton McCaffrey and colleagues at the university's medical school, encompassing the demonstration that delivery of synthetic small interfering RNA molecules to an adult mammal can induce in vivo silencing of a specific target gene. Financial terms were not disclosed.

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## OTHER NEWS TO NOTE

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• **Antigenics Inc.**, of New York, presented results from a Phase I trial of the company's personalized cancer vaccine, Oncophage (HSPPC-96), in patients with nonmetastatic pancreatic cancer, at the annual European Cancer Conference in Copenhagen, Denmark. In the pilot study that included 10 evaluable patients, patients in the trial experienced a median overall survival of 2.5 years, with one patient still alive and disease-free after more than five years, and two patients alive and disease-free 2.5 years and 2.2 years after treatment. Antigenics also presented findings from a Phase II trial of Aroplatin in metastatic colorectal cancer refractory to standard therapy. To date, one of the 15 evaluable patients has demonstrated a partial clinical response and two have experienced disease stabilization.

• **Asterand Inc.**, of Detroit, made available a new bank of material for researchers focused on eye diseases. The material could aid in research related to the genetic basis for a range of diseases, including glaucoma, advanced macular degeneration and diabetic retinopathy. The bank includes materials from systemic diseases affecting the eye such as vascular disease and hypertension.

• **Auxilium Pharmaceuticals Inc.**, of Norristown, Pa., reported long-term clinical data showing that treatment with Testim testosterone gel can significantly increase bone mineral density and improve body composition in aging hypogonadal men. In the open-label, multidose, multicenter study, 291 hypogonadal males with a mean age of 58 years were followed for 12 months. By month 12, following treatment with Testim gel at 100 mg/day, serum testosterone levels were in the normal range and the average bone mineral density of the lumbar spine rose 2.75 percent, a significant increase. Body composition also improved significantly with a 2.42 percent increase in lean body mass and 2.35 percent decrease in fat mass.

• **Biogen Inc.**, of Cambridge, Mass., said Avonex (interferon beta-1a) was shown to alter the long-term course of multiple sclerosis in patients who began treatment immediately after their initial MS attack, compared to initiation of treatment more than two years after onset of symptoms. The patients studied were considered at risk of suffering additional MS attacks because of the presence of brain MRI scan abnormalities. The study, known as CHAMPIONS (controlled high risk Avonex multiple sclerosis prevention study in ongoing neurological surveillance), was designed to determine whether the effect of early treatment with Avonex in delaying relapses and reducing the accumulation of MS brain lesions could be sustained for up to five years. The data were presented at the European Committee for Treatment and Research in MS meeting in Milan, Italy. Also, Biogen said the study would be extended for an additional five years.

• **Britannia Pharmaceuticals Ltd.**, of London,

entered an agreement with Novartis Pharmaceuticals Ltd., a subsidiary of **Novartis AG**, of Basel, Switzerland, to accelerate the development of dihydroergotamine (DHE) nasal powder, a formulation of DHE under development at Britannia since 2001. Britannia will use Novartis data to reduce the time to launch for DHE nasal powder in the UK in exchange for undisclosed milestone payments and royalties on UK sales. In addition, Novartis will be granted the first opportunity to license DHE nasal powder in countries outside of the UK. More specific financial terms were not disclosed.

• **Cardiome Pharma Corp.**, of Vancouver, British Columbia, said its heart failure drug candidate, oxypurinol, met the primary endpoint in a recently completed clinical trial. Results from the study confirmed preclinical and clinical studies showing the beneficial effects of oxypurinol on the endothelial dysfunction that often accompanies heart disease. Results from the EXOTIC study were presented at a satellite symposium during the Heart Failure Society of America's annual meeting. The primary endpoint of the study was reversal of acetylcholine-mediated coronary vasoconstriction after intravenous administration of oxypurinol. The study included 18 patients with coronary heart disease.

• **Cell Genesys Inc.**, of South San Francisco, said Chairman and CEO Stephen Sherwin will open the Nasdaq market today, celebrating Cell Genesys' 10 years on the exchange. The company focuses on cancer products.

• **Cellomics Inc.**, of Pittsburgh, reported the launch of the ArrayScan VTI HCS Reader, an automated, high-content screening (HCS) platform. The company also released three new BioApplication software modules for Cellomics' fully integrated HCS platform.

• **ChemCodes Inc.**, of Research Triangle Park, N.C., said it successfully completed a drug discovery collaboration with the preclinical research and development group of **F. Hoffmann-La Roche Ltd.**, of Basel, Switzerland. ChemCodes said the collaborative work allowed it to demonstrate its platform and medicinal chemistry capabilities in discovering new chemistries and synthetic routes for compounds required in lead generation. The partners said they would conduct a second collaboration as they continue to determine a specific therapeutic area, research plans and business arrangements. ChemCodes' platform uses components licensed from GlaxoSmithKline plc, of London.

• **Corixa Corp.**, of Seattle, and **GlaxoSmithKline plc**, of London, said data published in the Sept. 1, 2003, issue of *Blood* showed that therapy with Bexxar (tositumomab and I-131 tositumomab) following chemotherapy produced a high rate of response in patients with advanced follicular non-Hodgkin's lymphoma. The Phase II study, which assessed a two-part treatment consisting of CHOP chemotherapy (a combination chemotherapy regimen) followed by Bexxar, produced an overall response rate of 90 percent and a two-year overall survival rate of 97 percent.

## Financing

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postponed the pricing. The company expects the offering to close Thursday.

Pain Therapeutics' lead product is Oxytrex, which entered in June Phase III trials in chronic severe low-back pain. The company expects enrollment to take a year. Its product for irritable bowel syndrome, PTI-901, is expected to enter Phase III work in the fourth quarter.

At the end of the second quarter, Pain Therapeutics had \$42.5 million in cash and cash equivalents. It posted a net loss of \$4.3 million over that period and used 27.3 million shares outstanding to calculate its basic and diluted loss-per-share figures.

Citigroup Global Markets Inc., of New York, is sole book-runner on the offering and is joint lead manager, along with CIBC World Markets Corp., of New York. Leerink Swann & Co., of Boston, and ThinkEquity Partners LLC, of New York, are acting as co-managers.

### **Biomira Stock, Warrant Sale Expected To Raise \$16.3M**

Edmonton, Alberta-based Biomira Inc. said it arranged to sell 9 million shares and about 2.1 million warrants for about US\$16.3 million, giving it the funds needed to push its lead products.

The shares are priced at \$1.81, a 7.6 percent premium to the company's average closing price of \$1.68 on Nasdaq for the five trading days leading up to and including Sept. 18. Purchasers of common stock will receive 0.23 percent of one warrant for each share bought. Warrant holders will be entitled to buy one share of common stock at \$2.30. The warrants will expire Sept. 18, 2005, and there is a no-exercise period for six months.

Biomira's stock (NASDAQ:BIOM) fell 34 cents Monday, or 14.5 percent, to close at \$2. Rodman & Renshaw Inc., of New York, is acting as placement agent, and the financing is expected to close "at the earliest opportunity," the company said.

In June, the company reported that its lead product, Theratope vaccine, did not meet two primary endpoints in a Phase III metastatic breast cancer trial, although the company did see favorable trends in the data. A Phase II study in metastatic breast cancer continues, and the company expects to complete enrollment in 2004's first half. The vaccine, also being studied in colorectal cancer, is partnered with Merck KGaA, of Darmstadt, Germany. (See *BioWorld Today*, June 18, 2003.)

The company also is developing BLP25 Liposomal vaccine in non-small-cell lung cancer and prostate cancer.

For the three months ended June 30, Biomira posted a net loss of C\$5.5 million, or C9 cents per share. The company had C\$30.5 million in cash, cash equivalents and short-term investments at the end of the second quarter. It reported 56.9 million shares outstanding on a weighted average for the quarter.

### **Point Therapeutics Receives Agreements For \$11.2M**

Point Therapeutics Inc. has agreements to privately place units consisting of 5.6 million shares of stock and five-year warrants to buy another 2.8 million shares, which would raise \$11.2 million.

The per-unit purchase price represents a 12.5 percent discount to the average closing price of Boston-based Point's stock for the five trading days prior to Sept. 10. The warrants will be exercisable at \$2.66 per share.

Point's stock (OTC BB:POTP) fell 21 cents Monday to close at \$3.69.

New investor ProQuest Investments, of Princeton, N.J., will be included in the placement, as well as certain existing and new investors, Point said. The company is planning to use the funds for general corporate purposes and for clinical trials of PT-100, its lead product, which is being developed in a Phase I/II trial in combination with Rituxan (Genentech Inc.) in non-Hodgkin's lymphoma and chronic lymphocytic leukemia. It also is developing PT-100 in hematopoietic disorders caused by chemotherapy treatments.

As of June 30, the company had about \$7.8 million in cash, cash equivalents and marketable securities. It posted a net loss from operations of about \$1.7 million for the second quarter. Its basic and diluted weighted average shares outstanding for the quarter were about 9.3 million.

### **Neose Enters Agreements For \$23M Funding**

Neose Technologies Inc. said it has subscription agreements to sell shares in a registered direct offering at \$9 apiece, which would raise about \$23 million in aggregate proceeds. JP Morgan Securities Inc., of New York, is acting as placement agent. The financing is expected to close Thursday.

The company's stock (NASDAQ:NTEC) fell 15 cents Monday to close at \$10.10.

Horsham, Pa.-based Neose, which raised \$17 million in February, had \$42 million in cash, cash equivalents and marketable securities as of June 30. It lost \$9.2 million in the second quarter and reported weighted average shares outstanding of 17.2 million.

Neose focuses on improving therapeutics through its GlycoAdvance, GlycoPEGylation and GlycoConjugation technologies. It develops protein therapeutics that are designed to be improved versions of currently marketed drugs. The company said it would use the funds to strengthen its financial position as it pursues its own product development program.

Last month, Neose signed an agreement with Sandoz, a unit of Novartis AG, of Basel, Switzerland, in which Neose will use its technologies with a therapeutic recombinant protein supplied by Sandoz. If the companies elect to move ahead, they would share worldwide rights. ■

## Ambrx

*Continued from Page 1*

20 amino acids found in nature, its application results in the biosynthesis of proteins with new physical, chemical and pharmacological properties.

"About 18 months ago, it became clear to us that there was potentially a commercial opportunity that we should investigate," Wilson told *BioWorld Today*. "We got Dr. DiMarchi involved and the three of us began to define what the business opportunity would be and what the scientific objectives were going to have to be."

The trio opened Ambrx's doors in April, and soon after tapped Daniel for his clinical development background. Most recently, he had worked as the vice president of research for Amgen Inc., of Thousand Oaks, Calif. DiMarchi also brings protein commercialization experience to the table, given his most recent post as the group vice president for biotechnology and product development at Lilly Research Laboratories, a unit of Indianapolis-based Eli Lilly and Co. Schultz is a professor of chemistry at Scripps in La Jolla, Calif., as well as a director of the Genomics Institute of the Novartis Research Foundation. Wilson previously worked as the vice president of business development and the general counsel at the institute, part of Basel, Switzerland-based Novartis AG.

"With that, we felt that we had the team, technology and commercial opportunity – all the stars were lined up – and we went ahead with the financing after founding the company," Wilson said, adding that the funding would last about two years. "We have combined the strength of medicinal chemistry, the ability to incorporate building blocks that give you enhanced properties, with the commercial engine of protein biosynthesis."

Ambrx's early initiatives will apply the technology to proteins that already possess clinical data, but also well-established liabilities. Wilson declined to specify initial therapeutic areas of interest to the company, though he noted the technology is more focused on improving the properties of molecules rather than on specific therapeutic areas.

The technology could be used to make proteins orally available or more stable, allowing for storage without refrigeration. Ambrx's programs remain in preclinical development, with eventual plans to move products through more extensive development in partnership with larger collaborators.

"As a small biotech company, you really have to partner for a lot of reasons, such as financial, sophistication and market validation," Wilson said. "We're not going to try to do cookie-cutter deals, but we'd rather build several fairly focused relationships to bring value to that."

The company's financing round included 5AM Ventures, of Menlo Park, Calif., and Tavistock Life Sciences, of San Diego. Both venture capital firms also gained seats on Ambrx's board, including John Diekman, 5AM's managing

partner, and Shehan Dissanayake, Tavistock's CEO.

With its senior management team and several other key employees in place, Ambrx continues to recruit scientific and commercialization staff. Wilson said the company would grow to 25 to 35 employees by the end of next year.

"We're very focused on demonstrating both the scientific and commercial potential for the technology," he added. "Rather than telling people what we're going to do, we'd rather do it and let the data speak for us." ■

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## OTHER NEWS TO NOTE

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• **DanioLabs Ltd.**, of Cambridge, UK, entered a collaboration to use its inflammatory bowel disease model to screen compounds from a G protein-coupled receptor program belonging to **Oxagen Ltd.**, of Abingdon, UK. The compounds resulted from Oxagen's work to screen against inflammatory bowel disease-associated target receptors identified in its GPCR program. DanioLabs' model uses zebrafish as a model for human disease. Financial terms were not disclosed.

• **Depomed Inc.**, of Menlo Park, Calif., gained rights to a drug in development in its joint venture with **Elan Corp. plc**, of Dublin, Ireland, which at the same time withdrew its operational involvement in Depomed Development Ltd. As a result, Elan lost its right to exchange \$12 million of Depomed's Series A preferred stock for an additional 30.1 percent equity interest in the venture, though Depomed will continue to own its 80.1 percent share and the remaining 19.9 percent will be held by an Elan subsidiary. Depomed acquired exclusive development and commercialization rights to Gabapentin GR, a new formulation of the seizure and pain drug gabapentin that uses its controlled-release gastric retention drug delivery system. Depomed will not pay up-front license fees, but will pay undisclosed milestone and royalty payments to the joint venture if Gabapentin GR is successfully commercialized. Separately, Depomed filed a \$60 million shelf registration statement with the SEC to sell its common stock from time to time.

• **Elusys Therapeutics Inc.**, of Pine Brook, N.J., received an additional \$3.5 million from the U.S. Department of Defense to further develop its heteropolymer drug to remove anthrax toxin from the bloodstream. The company said the funding would allow it to complete final phases of its efficacy studies of the compound, ETI-205, and to scale up production in preparation for human safety studies. Elusys said previous government funds covered a significant portion of the preclinical development of the antibody drug, which is expected to remove the anthrax toxin from the bloodstream even after symptoms appear. Animal studies demonstrated that ETI-205 provides complete protection against a lethal anthrax spore challenge.

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## OTHER NEWS TO NOTE

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- **Endo Pharmaceuticals Inc.**, a wholly owned subsidiary of Endo Pharmaceuticals Holdings Inc., of Chadds Ford, Pa., said the FDA accepted the new drug application for DepoMorphine (morphine sulfate sustained-release liposome injection), an analgesic for the management of moderate to severe post-operative pain. Endo's development partner, **SkyePharma plc**, of London, submitted the application July 18.

- **Fluidigm Corp.**, of South San Francisco, said **GlaxoSmithKline plc**, of London, purchased its prototype Topaz AutolnspeX workstation and agreed to receive a supply of Fluidigm's disposable Topaz microprocessors. Fluidigm said GlaxoSmithKline has used the Topaz Crystallizer and its palm-sized microprocessors for screening of conditions that produce protein crystals, and now would use the complete Topaz system to optimize its crystallization operations as part of its drug discovery process. Financial terms were not disclosed.

- **Genomics Collaborative Inc.**, of Cambridge, Mass., said it was chosen by the Novartis Institutes for BioMedical Research Inc., a research institute of **Novartis AG**, of Basel, Switzerland, to collaborate in a large-scale human genetics research program to validate drug targets using GCI's database of human biological samples. The institutes and GCI scientists will work together to access GCI's Global Repository, a library of human DNA, serum and tissue samples all linked to clinical and demographic data, to help prioritize and gauge the potential success of drug targets before entering clinical trials. The nonexclusive research collaboration is for an initial two-year term, with the option to extend the program for two more years, and will cover up to four therapeutic areas, beginning with Type II diabetes.

- **Harvard Bioscience Inc.**, of Holliston, Mass., reported the acquisition, through its wholly owned Genomic Solutions subsidiary, of substantially all the assets of BioRobotics Ltd., a subsidiary of **Apogent Technologies Inc.**, of Portsmouth, N.H. The purchase price for the BioRobotics assets of about \$3.2 million is payable partly in cash and partly in the assumption of certain limited liabilities. BioRobotics designs, develops, manufactures and distributes life science instrumentation for DNA microarray manufacturing and colony picking.

- **Ingenuity Systems**, of Mountain View, Calif., said **GlaxoSmithKline plc**, of London, licensed part of its Knowledge Base technology to aid in internal development efforts of genome-scale computational solutions. The database includes biological networks created from millions of individually modeled relationships between proteins, genes, complexes, cells, tissues, drugs and diseases. Financial terms were not disclosed.

- **ISTA Pharmaceuticals Inc.**, of Irvine, Calif., presented integrated data from two Phase III trials of Vitrase (ovine hyaluronidase) for the treatment of vitreous hemorrhage, a condition affecting the back of the eye. A presen-

tation was made Sept. 20 at the annual meeting of the Retina Society in Chicago. The results were previously submitted to the FDA as part of a new drug application for vitreous hemorrhage. The company in August submitted a second NDA seeking approval for use of Vitrase as a spreading agent to facilitate the dispersion and absorption of other drugs. (See *BioWorld Today*, Aug. 6, 2003.)

- **Kucera Pharmaceutical Co.**, of Winston-Salem, N.C., received a research award from the North Carolina Biotechnology Center Small Business Innovation Research Bridge Fund Program related to its anti-HIV agent, KPC-2. The company, a 2001 spin-off of Wake Forest University Health Sciences and the School of Pharmacy at the University of North Carolina at Chapel Hill, said the funding would allow it to complete preclinical development of KPC-2, a compound for which it already received a Phase I SBIR grant from the National Institute of Allergy and Infectious Diseases, a unit of the National Institutes of Health in Bethesda, Md.

- **Micrologix Biotech Inc.**, of Vancouver, British Columbia, and **Fujisawa Healthcare Inc.**, of Deerfield, Ill., agreed to extend the review period on their collaboration and license agreement to Jan. 22, to further evaluate the available options based on analysis of the MBI 226 Phase III results. Under the agreement from July 8, 2002, Fujisawa has a right of termination that provides for a 60-day period for termination of the agreement following executive summary of the MBI 226 Phase III trial results. Prior to this extension, Fujisawa had until Sept. 22 to make its decision. MBI 226 did not demonstrate statistical superiority to povidone iodine in preventing catheter-related bloodstream infections.

- **Myriad Proteomics Inc.**, of Salt Lake City, changed its name to Prolexys Pharmaceuticals Inc. The name was chosen to more accurately reflect its corporate mission, it said. The company – co-founded by Hitachi Ltd., Friedli Corporate Finance, Oracle Corp. and Myriad Genetics Inc. – said it has made the conversion from a technology organization to a drug discovery company.

- **Netezza Corp.**, of Framingham, Mass., unveiled its Netezza Performance Server data warehouse for bioinformatics. Integrated with Blast and incorporating defined genomics data types, the NPS system is designed to deliver increased functionality and performance for large and complex bioinformatics analyses.

- **NPS Pharmaceuticals Inc.**, of Salt Lake City, presented interim results that suggest parathyroid hormone (PTH 1-84) might be more effective than the combination of PTH and alendronate, and alendronate alone, in promoting bone formation in post-menopausal osteoporotic women. The results came from a clinical study called PaTH (PTH/alendronate) presented at the 25th annual meeting of the American Society of Bone and Mineral Research in Minneapolis and published in the latest edition of *The New England Journal of Medicine*. The study lasted 12 months and involved 238 post-menopausal women with low hip or spine bone mineral density scores who had not been treated with alendronate.

## OTHER NEWS TO NOTE

• **Proneuron Biotechnologies Inc.**, of Los Angeles, obtained approval to begin a Phase II trial of Copolymer-1 (Cop-1) in Huntington's disease. The object of the trial will be to assess the safety, the immunological response and relevant efficacy parameters following the treatment of HD patients with Cop-1. The study will be conducted in Israel and will initially include 20 to 40 patients between the ages of 18 and 70.

• **Quantum Dot Corp.**, of Hayward, Calif., and **SC Biosciences Corp.**, **Matsushita Electric Industrial Co. Ltd.** and **Matsushita Kotobuki Electronics**, all of Tokyo, reported their first jointly developed product will be unveiled to drug discovery researchers this week at the Society for Biomolecular Screening annual meeting in Portland, Ore. The first product is a high-throughput optical scanner, with initial application in gene expression analysis. The product, called the Mosaic Scanner, is the first to be released under a collaboration between the companies reported on Aug. 6.

• **Receptor Biologix Inc.**, of San Francisco, licensed selected applications of its technology to **Incyte Corp.**, of Palo Alto, Calif. Incyte, which will use the license for its small-molecule cancer program, will make an undisclosed up-front investment along with future milestone payments and royalties in return for access to technology outside of Receptor's core business involving Intron Fusion Proteins. The newly founded company is working to develop a recently discovered class of protein therapeutics to treat cancer, autoimmune, metabolic and other diseases. Financial terms were not disclosed.

• **Sequenom Inc.**, of San Diego, reported the launch of the MassArray Compact system. The system analyzes DNA directly using mass spectrometry.

• **Sigma-Aldrich Corp.**, of St. Louis, said a Sunday morning explosion at its facility in Miamisburg, Ohio, injured one employee and resulted in a precautionary evacuation of those living within one mile of the plant. A nitric oxide tank exploded as employees, local firefighters and a hazardous material team were checking a leak at the plant, which is used to produce stable isotopes and isotopically labeled compounds used in life science research, medical diagnostics and positron emission tomography imaging. The facility containing the tank was largely destroyed.

• **Spectrum Pharmaceuticals Inc.**, of Irvine, Calif., and **GPC Biotech AG**, of Martinsried, Germany, said the FDA granted fast-track status to satraplatin as a second-line chemotherapy treatment for patients with hormone-refractory prostate cancer (HRPC). The companies are co-developing the drug. Satraplatin is a member of the platinum family of compounds and has completed the special

protocol assessment process with the FDA and is expected to enter a Phase III study in HRPC "in the near future," the company said. Spectrum's stock (NASDAQ:SPPI) rose \$2.26 Monday, or 46 percent, to close at \$7.17.

• **Teva Pharmaceutical Industries Ltd.**, of Jerusalem, reported data at the European Committee for Treatment and Research in Multiple Sclerosis conference in Milan, Italy, demonstrating that antibodies to Copaxone (glatiramer acetate injection) do not interfere with its biological functions. Other data demonstrated that long-term Copaxone treatment significantly reduces relapse rates and slows accumulation of disability for people with relapsing-remitting multiple sclerosis. More specifically, the findings demonstrated a reduction of sustained accumulated disability in patients who continued throughout the entire study follow-up period, which ranged from nine to 35 months.

• **Thermo Electron Corp.**, of Franklin, Mass., and **Qiagen NV**, of Venlo, the Netherlands, entered an exclusive agreement to co-market and co-promote Thermo Electron's KingFisher instrumentation technology together with Qiagen's magnetic bead-based nucleic acid separation and purification technology for use in nucleic acid-based applications in research and molecular diagnostics.

• **Titan Pharmaceuticals Inc.**, of South San Francisco, presented favorable results at the 25th annual meeting of the American Society For Bone and Mineral Research in Minneapolis, with oral gallium maltolate demonstrating the achievement of targeted, potentially therapeutic serum levels of gallium in patients with advanced Paget's disease. The trial evaluated the safety of gallium maltolate and gallium serum levels after oral administration of one of three doses, 200 mg, 400 mg or 600 mg, in 12 patients with advanced Paget's disease of bone or primary hyperparathyroidism. Results demonstrated serum gallium concentrations increased in a linear fashion with increasing doses.

• **Vitra Bioscience Inc.**, formerly Virtual Arrays Inc., of Mountain View, Calif., introduced the CellCard System and CellPlex Assays.

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## Lyme Disease

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controversy, scientists at Georgia Southern University in Statesboro tested the suspect carrier rats and mice for the presence of *Borrelia burgdorferi*. At least three rodent species were infected, as were three tick species, including deer ticks and two tick species, *Ixodes affinis*, not previously recognized as Lyme disease carriers.

The researchers report their findings in the *Proceedings of the National Academy of Sciences (PNAS)* published online the week of Sept. 16-19. Their paper is titled "An enzootic transmission cycle of Lyme borreliosis spirochetes in the southeastern United States." Its lead author is James Oliver and co-senior author F. W. Chandler.

Although the two newly discovered tick species rarely bite humans, the *PNAS* article suggests that the insects are important in preserving the disease presence in nature. Because the infection is maintained in these Southern states, human inhabitants there could be at risk for contracting Lyme disease, causing multisystem medical problems. The characteristic skin inflammation is usually accompanied by fever, malaise, fatigue, headache and stiff neck. Neurologic, cardiac or joint manifestations may occur weeks to months later.

Because of media coverage, Lyme disease has a higher profile than its occurrence warrants. Fewer than 18,000 cases are confirmed annually in the U.S. The patient fatality rate is virtually zero. Antibody studies in endemic areas indicate that as many as 50 percent of people who contract the infection never show symptoms. A separate survey, assessing the costs of misdiagnosing Lyme disease, found that 60 percent of patients referred to a Lyme disease clinic had never had the disease.

### Southern States Swing Bat Against Disease

"Our most important result," Oliver told *BioWorld Today*, "was we demonstrated that the species of spirochete causative of Lyme disease in the Northeastern and other areas of the United States [where it's most prevalent] is also found in the South, in this area. We proved it by isolating that particular spirochete in culture in the laboratory. And we obtained it from nature from three primary rodent reservoir hosts in which the tick vector usually feeds, so there is ample opportunity for the tick to pick the bacterium up.

"Also, we are finding further spirochetes closely related to the one causing clinical Lyme disease. We find them in the South as well. Microbiologists differentiate them as 'genospecies.' We found three genospecies of spirochetes that cause Lyme disease. Until 10 years ago all were considered one species.

"There is more genetic diversity in the South where the disease is not so common as in the North where it is quite widespread," Oliver continued. "An interesting twist: Less genetic diversity in the North but the one that most

often causes human disease is now often found in the South. These rodents, we show, live for an unexpected long time in captivity. We pamper them in the lab – air conditioned, plenty of food, no predators. I would expect them to live one or two years but some of them live five or six years. We showed that these three species of rodents – cotton rats, cotton mice and wood rats – are very good hosts for ticks and spirochetes. That means if *scapularis* is feeding on non-*scapularis* hosts, then the prevalence of infection is very low, whereas in the North it's quite high, with many more people in the North dead than in the South.

"In 'true' Lyme disease the symptoms are the same," Oliver observed, "but we don't have it in the numbers and it's not nearly the problems they have in the North, the Lyme 'hot strains.' I think the main thing is that we have not isolated the *Borrelia burgdorferi* spirochete from ticks and rodents to human patients. For one thing, it's not as common. For another, people and physicians are aware of Lyme disease, so when they get the first symptoms, they treat it immediately. And fortunately for us, antibiotics work very well on Lyme disease, and get rid of it in most cases. So we don't see progression of disease because it progresses only from mice."

### Physicians Told Lyme Disease Won't Grow In South

"In the North where most of the original early work was done, there were a lot of patients there who went from first to second to third stage where arthritis, particularly in the knee and major joints, is very common and debilitating. In the South there is some indication that the people who had gotten over Lyme disease, for whatever reason, don't as often develop these chronic arthritic, crippling-type conditions. It's a situation in the South where physicians were told early that it didn't occur in the South. A lot of them make that a diagnosis on eliminating other diseases until they get down to a particular ailment. So they rule out the possibility of Lyme disease

"We did do one study," Oliver went on, "where we had some patients, tried to isolate the spirochete and failed. That makes me think there are some strain differences there between Southern and Northern spirochetes. But on the other hand we know that spirochetes are very fastidious about growing conditions. So our failure to isolate them in culture medium is not all that surprising. We failed with a small group of patients but this needs large numbers before we can make a conclusion. That's one of the problems of Lyme disease all along. People make conclusions on the basis of data but not enough data.

"We took a little biopsy out of one patient, plopped it into growth medium but it just didn't grow. Yet the patients had the bull's-eye lesions of classical first-phase Lyme disease, [but] were treated right away so they didn't develop subsequent infections," Oliver concluded. ■