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PAGE 1 OF 8

Arena Defends New Phase III Data, Plans Lorcaserin Path

By **Trista Morrison**
Staff Writer

Arena Pharmaceuticals Inc. released data from its Phase III BLOOM-DM trial of weight loss drug lorcaserin in obese and overweight diabetics on Tuesday, sparking plenty of debate among analysts and investors about whether the new findings would help – or hurt – the company’s chances at addressing issues raised in an FDA complete response letter last month.

On the efficacy front, the FDA wants obesity drugs to show either 5 percent placebo-adjusted weight loss or twice as many patients losing 5 percent of their weight on drug vs. placebo. Lorcaserin has come under fire for consistently achieving the latter but not the former, and the new data were no different.

In its first two Phase III trials, BLOOM and BLOSSOM, lorcaserin delivered placebo-adjusted weight loss of 3.6

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Pfizer Seeks New Indications Using Biovista Bioinformatics

By **Catherine Shaffer**
BioWorld Today Contributing Writer

A research collaboration between Pfizer Inc. and Biovista Inc. will seek new indications for Pfizer drug candidates in development using a bioinformatics technology platform developed by Biovista. Terms of the agreement include identification of up to three new indications for each drug. Biovista will receive an undisclosed up-front payment and success milestone payments.

“Pfizer enjoys a significant leadership in the pharmaceutical industry in terms of wishing to systematically explore new uses of its drugs,” Aris Persidis, president of Biovista, told *BioWorld Today*.

Pfizer, of New York, established its Indications Discovery Unit in 2007 to reposition failed compounds and identify additional indications for compounds in

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Clogging Up the Plumber

Chemotherapy Can Contribute to Resistance to Itself

By **Anette Breindl**
Science Editor

Beating cancer is a frequent occurrence – but often, only for a time. Drugs that work initially stop being effective, which all too frequently means that remission comes to a bitter end.

Research published this week showed that in some cases, jamming a specific DNA repair mechanism may prevent cancer cells from developing resistance to chemotherapy. Inhibiting so-called translesional DNA repair may provide a useful addition to some frontline chemotherapies.

Why cancer cells become resistant to chemotherapy drugs is still not fully understood. One idea is that chemotherapy selects for cells that are intrinsically resistant: First-round chemotherapy will kill the 99 percent of cells that are sensitive to it, allowing a patient to go home

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Gates: Vaccine Innovation, Delivery Key to Global Health

By **Donna Young**
Washington Editor

WASHINGTON – While the development of new drugs in general has experienced little progress over the past decade, innovation in vaccines and specific treatments, like HIV/AIDS therapies, has had a “great period of productivity,” said Microsoft Corp. founder Bill Gates, co-chair of the Bill & Melinda Gates Foundation.

He noted that the number of children dying worldwide by age 5 has dramatically dropped from 20 million per year in the 1960s to 8.5 million currently – largely due to better vaccines and greater global immunization rates.

“Smallpox has gone from killing 2 million per year to zero per year, and measles has gone from 1.5 million deaths to 300,000” per year worldwide, Gates said Tuesday at the 2010 mHealth Summit, which brought

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ACR Roundup

The following data were presented at the American College of Rheumatology meeting in Atlanta. (Also see page 4.)

- **ChemoCentryx Inc.**, of Mountain View, Calif., said positive Phase I data for CCX354, an oral, small molecule designed to target the chemokine receptor CCRI, showed an excellent safety profile in healthy volunteers, as well as in rheumatoid arthritis patients. Pharmacokinetic data showed once-daily doses of CCX354 produced greater than 90 percent receptor coverage on blood leukocytes throughout the day.

- **Horizon Pharma Inc.**, of Northbrook, Ill., said results from a long-term safety study of HZT-501, a single-tablet formulation of ibuprofen and high-dose famotidine, showed that the drug's safety was comparable to ibuprofen alone. Data also showed that HZT-501 was associated with a two-fold reduction in the incidence of dyspepsia compared to ibuprofen alone, although not statistically significant due to small sample size. The firm also presented data from its two pivotal studies of Lodotra, a modified-release formulation of prednisone, showing that a statistically significant and clinically relevant higher response rate evaluated by ACR response criteria in rheumatoid arthritis (RA) patients treated with 5 mg of Lodotra compared to placebo, in addition to standard RA therapy, after 12 weeks of treatment.

- **Idera Pharmaceuticals Inc.**, of Cambridge, Mass., reported preclinical data showing that its IMO-3100, a Toll-like receptor antagonist, suppressed immune responses mediated through TLR7 and TLR9, reducing the production of cytokines such as tumor necrosis factor-alpha, interleukin-6, IP-10 and interferon-alpha in cells isolated from blood samples. TLR7- and TLR9-mediated immune responses remained suppressed by weekly IMO-3100 administration throughout the four-week treatment period. Data from another preclinical study showed that blood cells from healthy females produced higher levels of pro-inflammatory cytokines in response to TLR7 stimulation than do blood cells from healthy male subjects.

Coming Thursday in *BioWorld Perspectives:*

New Technology Must Be Used to Steer Students to High-Tech Careers

What and where are the hot jobs in the life sciences during the next decade? And will there be enough trained applicants to fill these positions? . . . Tune in to this week's *BioWorld Perspectives* in which Contributing Writer Ilene Schneider discusses the top fields in life sciences and what it will take to get students interested in science.

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Stock Movers

11/9/10

| Company | Stock Change | |
|-------------------------------|--------------|--------|
| Nasdaq Biotechnology | -\$8.07 | -0.9% |
| Aastrom Biosciences Inc. | +\$0.43 | +12.7 |
| BioCryst Pharmaceuticals Inc. | -\$0.36 | -6.6% |
| Genomic Health Inc. | +\$3.09 | +20.6% |
| Metabolix Inc. | -\$2.72 | -19.8% |
| Orexigen Therapeutics Inc. | -\$0.56 | -9.1% |
| Santarus Inc. | -\$0.28 | -8.5% |

(Biotechs showing significant stock changes Tuesday)

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Arena

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percent and 3.1 percent, respectively. In the BLOOM-DM trial, lorcaserin patients achieved 4.5 percent mean weight loss compared to 1.5 percent for placebo, resulting in placebo-adjusted weight loss of 3 percent.

In BLOOM and BLOSSOM, 47.5 percent and 47.2 percent of lorcaserin patients lost more than 5 percent of their weight, approximately double the 20.3 percent and 25 percent for placebo patients, respectively. And in the new BLOOM-DM study, 37.5 percent of lorcaserin patients lost more than 5 percent of their weight, compared to 16.1 percent of placebo patients.

Technically, companies need to satisfy only one – not both – of the FDA's efficacy requirements, which Arena has done. But FDA briefing documents ahead of a recent advisory committee meeting said the efficacy criteria were met only by a "slim margin," and the FDA reiterated its opinion that lorcaserin's efficacy is "marginal" in its complete response letter. (See *BioWorld Today*, Sept. 15, 2010, Sept. 17, 2010, and Oct. 26, 2010.)

Leerink Swann analyst Steve Yoo wrote in a research note that the BLOOM-DM data "may do little to alter that perception."

Yet Arena President and CEO Jack Lief disagreed. "We believe these results address the weight management challenges of patients with diabetes," he told *BioWorld Today*, adding that diabetics typically have a hard time losing weight, so the fact that lorcaserin's efficacy in these patients was fairly in line with its efficacy in nondiabetics is "really good." Lief also pointed to data showing that lorcaserin reduced HbA1c levels by 0.9 percent compared to 0.4 percent for placebo ($p < 0.0001$), with half of the lorcaserin patients getting their HbA1c level below the recommended 7 percent goal, compared to only one-quarter of placebo patients. That's a "really big deal," he said.

Rodman and Renshaw analyst Elemer Piros noted, however, that the drug did not significantly improve fasting insulin, triglycerides, cholesterol levels or blood pressure, which Piros said "further questions the clinical significance of the efficacy findings." Lief argued that improvements were seen on "virtually all" of the secondary endpoints, although the small size of the trial may have complicated statistical significance.

Yet it has been safety, not efficacy that has proven the bigger stumbling block for lorcaserin lately, and the BLOOM-DM data raised additional questions in that department.

The most common adverse events in the trial were headache, upper respiratory infection, back pain and nasopharyngitis. But Arena also said 2.9 percent of lorcaserin patients and 0.5 percent of placebo patients had new valvulopathy at week 52, although the study was not powered to detect meaningful differences in valvulopathy.

That tid bit had some investors fired up because there was less valvulopathy disparity between the lorcaserin

and placebo groups in the BLOOM and BLOSSOM trials. Any valvulopathy signal is likely to spook investors because lorcaserin is a 5-HT_{2C} agonist specifically designed to avoid the valvulopathy issues of 5-HT_{2B} agonists like Wyeth's infamous Fen-Phen (dexfenfluramine/phentermine).

The Fen-Phen ghost spooked a few of the FDA's reviewers, too, but the agency didn't raise the issue in its briefing documents or complete response letter, so Yoo said it is "unlikely to become an issue" now. Lief added that BLOOM-DM was a much smaller trial than the other two, and "a couple of patients can move the percentages in a large amount."

Yoo and other analysts remained focused on the preliminary safety issue raised by both the FDA and its advisors: preclinical cancer signals in rats. Arena has always maintained that the rat data have no relevance to humans, and Lief said no cancer signal has been detected in any of lorcaserin's clinical trials, including BLOOM-DM. But the company will have to convince the FDA.

Arena and partner Eisai Inc. have a meeting with the FDA scheduled to discuss the complete response letter before the end of the year.

Shares of San Diego-based Arena (NASDAQ:ARNA) fell 5 cents to close at \$1.48 Tuesday. The company reported that it had \$176.5 million in cash as of Sept. 30, after posting a net loss of \$36.3 million for the third quarter.

Vivus Inc. also received an FDA complete response letter for obesity drug Qnexa (phentermine/topiramate) last month. Orexigen Therapeutics Inc.'s obesity drug Contrave (naltrexone SR/bupropion SR) will face the FDA's panel next month. (See *BioWorld Today*, Nov. 1, 2010.) ■

Clinic Roundup

- **Amgen Inc.**, of Thousand Oaks, Calif., reported that denosumab was superior to Zometa in preventing skeletal-related events in breast cancer patients with bone metastases. The Phase III study included 2,046 patients. Results were published in the *Journal of Clinical Oncology*.

- **Ardea Biosciences Inc.** reported that its investigational drug RDEA594 in combination with febuxostat (Uloric) or allopurinol reduced uric acid levels in patients with gout to a greater degree than either of the marketed drugs alone. The San Diego-based company completed enrollment in a Phase IIb study of RDEA594 with allopurinol in gout patients who failed allopurinol alone.

- **Argos Therapeutics Inc.**, of Durham, N.C., said data from a Phase IIa trial of ARS-004, its Arcelis HIV program, demonstrated a significant reduction in viral load and a delay in viral rebound kinetics during a 12-week antiretroviral treatment interruption when compared to pre-ART viral loads. ARS-004 currently is in testing in a Phase IIb study co-funded by the National Institutes of Health. The Arcelis technology is designed for personalizing RNA-loaded dendritic cell immunotherapies.

Biovista

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ongoing development. One of the most notable examples of drug repositioning was sildenafil citrate (Viagra), which was being developed as an angina drug and was repositioned to the indication of erectile dysfunction.

The concept behind drug repositioning is that disease pathways share druggable targets, and so a drug that seems to hit a target well, but fails for its intended disease indication, may be successful in another indication relevant to the same target.

And that's where Biovista comes in.

Persidis prefers not to refer to Charlottesville, Va.-based Biovista's Clinical Outcome Search Space (COSS) technology as software.

"We don't call it software because it isn't just software," Persidis said. "It's a technology platform that matches the very deep description of the mechanism of action of every drug against every one of the 23,000 diseases and 6,000 adverse events tracked by medicine." (See *BioWorld Today*, Oct. 7, 2009.)

A typical COSS treatment for an individual drug will take 30 to 60 days. The automation portion of the system conducts real-time assays of the drug against its database of mechanisms and targets. After the initial data are returned, a team of therapeutic area experts processes the information.

The system differs substantially from a data mining application, which only turns up results that are present in the database. COSS creates results based on information in the database, which was created using a mix of publicly available data and proprietary data owned by Biovista or its collaborator.

Biovista validated COSS using its own internal pipeline of compounds, including BVA101 and BVA201 in multiple sclerosis, BVA601 in epilepsy, BVA501 and BVA701 in glioblastoma multiforme and melanoma.

Biovista said that in 2009, it used COSS to file intellectual property claims for more than 60 drugs in nine different indications including epilepsy, multiple sclerosis, advanced macular degeneration, Sjögren's syndrome, Hodgkin's lymphoma, multiple myeloma, diabetes, thyroid cancer and bone disorders.

In addition to the new collaboration with Pfizer, Biovista has an existing relationship with the FDA's Office of Clinical Pharmacology. In January 2010, the FDA announced that it had licensed Biovista's technology to help it analyze harmful side effects in drugs.

"We've been informally collaborating with the FDA for at least four years," said Persidis.

Pfizer is working with a number of other partners to explore new indications for its compounds. In May 2010, Pfizer announced a collaboration with Washington University School of Medicine in St. Louis to attempt to reposition more than 500 compounds. Under the five-year,

\$22 million agreement, Washington University scientists will review research data on drug candidates that currently are or have been in clinical trials.

Another drug repositioning partnership with Gene Logic Inc. by Pfizer produced a milestone payment in 2007 triggered by a patent application. ■

ACR Roundup

- **Tonix Pharmaceuticals Inc.**, of New York, said results of a new analysis from a Phase IIa study showed that bedtime administration of very low dosage cyclobenzaprine was associated with reductions in an objective measure of non-REM sleep instability, and those reductions were statistically significantly correlated with diminished pre-sleep/p.m. fatigue in fibromyalgia syndrome. Previous data showed that the drug reduced pain, fatigue and tenderness in patients with FMS.

- **UCB SA**, of Brussels, Belgium, and **Immunomedics Inc.**, of Morris Plains, N.J., said results from the Phase IIb EMBLEM study showed that certain doses of epratuzumab were associated with a meaningful and statistically significant reduction in disease activity in adult patients with moderate to severe active systemic lupus erythematosus. All dose ranges from 200 mg to 2,600 mg administered during one 12-week treatment cycle had numerically superior response rates compared to placebo at week 12, and for patients receiving epratuzumab at a cumulative dose of 2,400 mg, there were meaningful and statistically significant reductions in SLE disease activity, with responder rates more than double those of placebo. In separate news, UCB reported data showing that the addition of Cimzia (certolizumab pegol) to current therapy was associated with a rapid clinical response, improved function and reduced disease activity in a diverse group of adult rheumatoid arthritis patients. The 12-week Phase IIIb trial met its primary endpoint, with 51.1 percent of patients in the Cimzia group achieving ACR20 score vs. 25.9 percent in the control group.

Other News To Note

- **Acadia Pharmaceuticals Inc.**, of San Diego, has been awarded a grant from The Michael J. Fox Foundation for the development of Nurrl-RXR agonists for the treatment of Parkinson's disease. The company said that the grant of \$300,000 was awarded under the foundation's Therapeutics Development Initiative aimed at supporting preclinical development of Parkinson's disease therapies that have the potential for fundamentally altering disease course and improving treatment of symptoms above and beyond current standards of care. The grant is Acadia's third award from the foundation.

Chemotherapy

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with no overt signs of disease, but with a small reservoir of resistance cells left over that can pick up where they left off, repopulating the tumor.

But there is also suspicion that chemotherapy itself contributes to cancer cell resistance. "A lot of these chemotherapeutic agents are DNA-damaging agents," Graham Walker told *BioWorld Today* – and DNA damage is what is at the root of cancerous changes in the first place.

In a paper published in the Nov. 8, 2010, online edition of the *Proceedings of the National Academy of Sciences*, Walker, who is an American Cancer Society research professor of biology at the Massachusetts Institute of Technology and a member of the Howard Hughes Medical Institute, and colleagues confirmed that standard chemotherapy can indeed induce resistance to themselves in cancer cells. They also identified a key cellular process in the induction of such resistance, and suggested inhibiting this process might be a way to prevent such resistance from emerging.

The process Walker and his team set their sights on is translesional DNA synthesis, a DNA repair mechanism that is unique in that it can introduce mutations even as it is repairing DNA. As a rule, copying DNA needs to be an exact process, and so normal DNA polymerases – the enzymes that do the copying – are a finicky bunch. Anything unusual – missing bases, but also bridges between base pairs that can be induced by ultraviolet light – will cause them to abandon their attempt to replicate DNA, which ultimately dies if it cannot divide.

Translesional DNA repair, Walker said, is carried out by "special classes of DNA polymerase that have a more flexible and spacious active site." It can help cells survive when their DNA is under assault – but at the cost that "now you could put mutations in at the same moment you are repairing the DNA."

Walker, co-corresponding author Michael Hemann, and their colleagues looked at the relationship between chemotherapy, resistance and translesional synthesis because it is the most error-prone way of copying DNA. "There are lots of ways to repair [DNA] accurately," Walker said, "but only one major way to put in mutations."

In their papers, the authors looked at Rev1 and Rev3, which are subunits of two different translesional DNA polymerases, though Walker said they tend to act in concert as part of the same pathway.

In mice with lymphoma, Walker and his team demonstrated through serial transplantation experiments that chemotherapy treatment led to mutations that made some cells resistant to the chemotherapy. Inhibiting translesional repair while administering the chemotherapy reduced resistance, as well as tumor spread more generally.

In a companion paper, they also showed that inhibiting the same enzyme can overcome intrinsic resistance, that is, resistance not caused by the chemotherapy itself. In this set

of experiments, inhibiting translesional repair in animals with an aggressive form of lung cancer that was resistant to cisplatin sensitized the animals to the chemotherapy, doubling their survival times.

Collectively, the authors wrote, the studies suggested that "a treatment strategy based on pairing a DNA-damaging chemotherapeutic agent . . . with a drug that inhibits the mutagenic [translesional synthesis] pathway could be very powerful, because it could reduce significantly the rate at which cells acquire chemoresistance."

Walker said that his team is currently searching for inhibitors that could be used in any future clinical studies, as well as delving into the basic biology of "which characteristics of the cancer would make it amenable to this approach."

"Not all cancers are going to depend on translesional synthesis to keep themselves alive," he said, so "the hope would be to try to identify cancers would be susceptible." Certain cancer cell lines express the polymerases in question at very high levels, suggesting that they might be good candidates for such a combination approach.

Toxicity would also be a bigger concern with this approach than with more targeted therapies, since inhibiting DNA repair would also affect healthy cells. Walker said that this is why it is important to look for cancers that rely heavily on translesional repair. For such cancers, there is more likely to be a therapeutic window where inhibiting this mechanism kills cancer cells, while normal cells are "better able to shrug it off" and rely on alternate DNA repair mechanisms.

Walker noted that clinical trials are a good way off at best, but said the results his team has published are encouraging enough to pursue the idea further – "and keep our fingers crossed." ■

Clinic Roundup

- The FDA informed **Endo Pharmaceuticals Inc.**, of Chadds Ford, Pa., that it will not be necessary to convene a joint meeting of the Anesthetic and Life Support Drugs Advisory Committee and Drug Safety and Risk Management Advisory Committee to review its new drug application for long-acting oxymorphone for moderate to severe chronic pain. The agency is able to make its decision based on previous advisory committee meetings.

- **Nabi Biopharmaceuticals Inc.**, of Rockville, Md., completed enrollment of a second Phase III trial of NicVAX, a nicotine conjugate vaccine for nicotine addiction. The new trial will evaluate abstinence from smoking over a 12-month period in 1,000 patients. Secondary endpoints include abstinence rate at various intervals, safety and immunogenicity of the vaccine, withdrawal symptoms, cigarette consumption, smoking satisfaction and nicotine dependency. The first Phase III trial completed enrollment in July, with final data expected in the fourth quarter of 2011. Results from the latest trial are expected in early 2012.

Global Health

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together health and technology leaders, researchers, policymakers and community groups to discuss the use of wireless technology for improving global health.

He insisted that vaccines for diseases, such as malaria, respiratory illnesses and viral diarrhea, will not only be the key to improving global health, but in reducing poverty and raising productivity.

Cutting the number of worldwide deaths – particularly in developing nations – also will reduce population growth, Gates argued, noting that such an assertion “sounds paradoxical.”

“The fact is,” he said, improving health outcomes results in parents in poorer nations having fewer children.

Gates noted that one southern region of India with healthy residents has experienced a low population growth in recent years, while a northern region, where vaccines, therapies and other health care is less accessible, has seen a 3 percent annual growth in population.

“No matter what problem you care about, the key thing is those problems are insoluble at 3 percent growth rate,” he said. “Nobody can handle that type of situation.”

Whether it is energy, biology or robots, Gates said most people underestimate the amount of innovation currently under way.

He said the greatest medical challenge currently facing the planet is not a new disease, but the “tough time” for foreign aid for vaccines and other global health care programs, with many governments slashing their budgets, which Gates said may lead to a stifling of medical innovation.

He noted that Italy recently cut its foreign aid for health care and other programs in half.

“I hope it doesn’t get cut in the U.S., but I’m quite concerned it will be,” Gates lamented.

He added that the UK has so far been able to avoid cutting any foreign aid for health care.

“In general, the world underfunds research,” Gates said.

Nonetheless, he praised the U.S. as being “exemplary” for providing the National Institutes of Health with a \$30 billion budget, which he noted largely goes to basic and early research.

While Gates said he supported capitalism – “it’s better than government” – he noted that there is some research that the private sector just would not fund.

On the same day he spoke in Washington, Gates’ foundation revealed 65 new winners of its Grand Challenges Explorations global health project grants.

Initial grants of \$100,000 are awarded two times a year, with successful projects having the opportunity to receive a follow-on grant of up to \$1 million under the five-year \$100 million Gates Foundation initiative.

Some of this year’s recipients included an Ohio State researcher who is developing a safe strain of the tuberculosis bacterium for use in fermenting beans in a

traditional Asian dish, known as natto, which could then be eaten as an oral TB vaccine.

Chicago-based VaxTrac Inc. also won a grant to test a mobile phone-based vaccination registry, which uses fingerprint scans to track those who have received immunizations in hopes of reducing redundant doses and boosting coverage levels in developing countries.

While the focus of the mHealth Summit was advancing the use of cell phones, the Internet and other wireless technologies to improve global health, Gates cautioned that “We have to approach these things with some humility,” noting that despite the rapid progress of mobile technologies, using them for health care delivery in some areas of the world without reliable electricity or cellular towers may not yet be feasible.

He contended that the best environment to test health care innovation is “middle income” countries, such as Brazil or China.

While rich countries, like the U.S., spend “huge amounts of money on its health system,” it also is heavily regulated, with a “very strange” incentive system, such as better reimbursements for acute care than for preventive care, which is less costly in the long run.

Also speaking at the mHealth Summit Tuesday was media mogul and billionaire Ted Turner, who said his best advice to innovators and entrepreneurs, was “early to bed, early to rise, work like hell and advertise.”

Turner said he has experienced the same type of skepticism that all start-ups face, not just when he founded CNN as an entrepreneur, but when he gave \$1 billion to establish the United Nations Foundation, a nonprofit charitable organization that advocates for the UN in solving global problems.

“It’s hard to raise capital when you don’t have an established track record,” Turner said.

Nonetheless, he said, “there are fewer barriers” in the business world than when he got started, “which is good.” ■

Clinic Roundup

- **NeuroDerm Ltd.**, of Ness Ziona, Israel, started a Phase IIa trial of ND0801, a dermal patch based on a combination with nicotinic actions, in attention deficit disorders/attention deficit hyperactivity disorder in adults. The study is expected to enroll 45 subjects and will examine safety, tolerability and optimal therapeutic dose, as well as evaluate the cognitive improvement.

- **Nuvo Research Inc.**, of Mississauga, Ontario, reported that its investigational drug WF10 for allergic rhinitis met its primary endpoint in a Phase II trial carried out in Leipzig, Germany. In 60 patients with a two-year history of persistent allergic rhinitis and positive skin allergen test, treatment with WF10 resulted in a significant change in Total Nasal Symptom Score without significant adverse events.

Other News To Note

- **Advanced Life Sciences Holdings Inc.**, of Chicago, submitted a proposal to the National Institute of Allergy and Infectious Diseases for a biodefense contract that would advance development of intravenous antibiotic Restanza (cethromycin) for bioterror pathogens. The drug is also in a Phase III trial for community-acquired bacterial pneumonia following the receipt of a complete response letter last year. (See *BioWorld Today*, Aug. 11, 2010.)

- **Aposense Ltd.**, of Petach-Tikva, Israel, signed a deal for **Roche AG**, of Basel, Switzerland, to use its EarliTest solution with the oncology program at Roche. Data generated from the collaboration will provide an opportunity for the companies to expand the use of EarliTest to oncologic therapies. Under the terms of the nonexclusive agreement, Roche will fund the clinical trials and pay Aposense undisclosed license and milestone fees.

- **AtheroNova Inc.**, of Irvine, Calif., signed a research agreement for the second phase of a preclinical laboratory study with Cedars-Sinai Heart Institute's Division of Cardiology. The protocol for the study is to validate results from initial preclinical testing that showed 95 percent less occurrence of arterial plaque compared to the control group.

- **Chimerix Inc.**, of Research Triangle Park, N.C., reported data from in vitro studies showing that antiviral agent CMX001 selectively inhibited the replication of human polyomavirus JC, the cause of progressive multifocal leukoencephalopathy, in immunocompromised or immunosuppressed patients. The effect of CMX001 on JCV replication using human glia-derived cells was investigated, with data showing that extracellular JCV was reduced by 50 percent by CMX001 in glia-derived cells. Data also showed the drug's benefit in monkey cell lines COS-7 cells. Those results were presented at the Antiviral Congress in Amsterdam, the Netherlands.

- **CMDBioscience LLC**, of Orange, Conn., completed a research collaboration aimed at identifying peptide antagonists of the dengue virus using its computational peptide drug discovery platform. Scientists were able to model and optimize a structure of the dengue viral target and evaluate more than 480,000 peptide ligand sequences, ultimately converging on the 27 most promising sequences. Subsequent synthesis and testing revealed anti-infective activity for five of the designed peptide ligands.

- **EUSA Pharma Inc.**, of Oxford, UK, submitted a biologics license application for Erwinase (L-asparaginase derived from *Erwinia chrysanthem*) for use in acute lymphoblastic leukemia patients with hypersensitivity to *E. coli*-derived asparaginase. The application is being submitted on a rolling basis, following receipt of fast-track status from the FDA, and the BLA requests a six-month priority review.

- **Fabrus LLC**, of La Jolla, Calif., has started a research program with **Ambrx Inc.**, of San Diego, to discover antibodies with properties that are optimized for use as antibody drug conjugates. Under the research agreement, Fabrus will use its antibody library, screening and functional maturation approaches to deliver affinity-matured antibodies against a number of targets nominated by Ambrx. The collaboration antibodies will be modified by Ambrx, using its unnatural amino acid technology, to produce antibody drug conjugates directed to each therapeutic target. The agreement grants Ambrx the exclusive right to commercialize conjugated forms of the antibodies generated under the collaboration. Fabrus will receive various up-front payments and is eligible to receive success fees and a share of certain payments received by Ambrx in the future. Ambrx was granted an option to acquire a minority equity interest in Fabrus. (See *BioWorld Today*, Aug. 18, 2010.)

What You Missed in BioWorld Insight Monday

FDA Approval: Not the End Game Anymore

It used to be that getting a drug approved was the most important thing a drug developer had to do. But recently, several biotechs have won approval only to run into trouble getting their drugs paid for – a problem that is likely to intensify thanks to comparative effectiveness. And when patients aren't buying, potential partners aren't likely to buy either.

The Strategy Behind Maxygen's Midas Touch

The interesting thing about Maxygen Inc.'s recent platform technology sale is that the biotech didn't need the cash. In fact, Maxygen has so much money that it has handed some \$40 million back to investors over the past year – something rarely seen in the biotech world. How did Maxygen end up in this enviable position, and what happens when it runs out of assets to monetize?

Experts Provide Insider Tips for Going from Start-Up to Success

At law firm Foley & Lardner LLP's annual life science conference, a panel of biotech experts guided two fictional scientists through starting a biotech. From a breakdown of valuations to tips for accelerating the patent process and landing a partner, the panel provided both the basics and several surprises.

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Other News To Note

• **GenVec Inc.**, of Gaithersburg, Md., said Nasdaq granted the firm an additional 180 days to regain compliance with the minimum \$1 bid price rule for continued listing. GenVec now has until May 9, 2011.

• **Immunologix Inc.**, of Charleston, S.C., entered a deal with contract research organization **GenScript**, of Picataway, N.J., to offer a complete platform for producing human antibody therapeutics. Financial terms were not disclosed.

• **Immunovaccine Inc.**, of Halifax, Nova Scotia, reported that a preclinical study testing the efficacy of combining its DepoVax with CEL-2000, a rheumatoid arthritis vaccine antigen from **CEL-SCI Corp.**, of Vienna, Va., showed a single-dose of the combination product considerably lessened the symptoms and slowed the progression of rheumatoid arthritis in an animal model.

• **Insight Genetics Inc.**, of Nashville, Tenn., was awarded a \$200,000 Phase I Small Business Innovation Research contract from the National Cancer Institute to develop a companion diagnostic for lung cancer patients. As part of the contract, the company will further validate its ALK Screen real-time PCR-based test, which is aimed at detecting cancer-causing fusions and mutations of anaplastic lymphoma kinase, using lung cancer specimens. About 5 percent to 10 percent of lung cancers are caused by ALK mutations.

• **Omeros Corp.**, of Seattle, announced that a compound identified by the company as an antagonist of GPR87, an orphan GPCR recently unlocked for drug development by Omeros and linked to squamous cell carcinoma, potentiates the tumor-killing activity of doxorubicin (Adriamycin), a widely used chemotherapeutic agent. The company said it is the first compound in a series of GPR87 antagonists exclusively identified by Omeros that the company has evaluated in proof-of-concept models. Omeros said that it is initiating medicinal chemistry optimization of the compound. (See *BioWorld Today*, Oct. 26, 2010.)

• **PolyMedix Inc.**, of Radnor, Pa., announced that data from two separate preclinical research studies were published in the December 2010 issue of *Molecular Oral Microbiology* and, according to the company, demonstrated that investigational defensin-mimetic compounds exhibited both anti-inflammatory and antimicrobial activity against microbial biofilms that cause infections of the oral cavity. It is the first scientific publication of the discovery of anti-inflammatory activity with PolyMedix's defensin-mimetic compounds, the company said.

• **Repros Therapeutics Inc.**, of The Woodlands, Texas, said the FDA recommended during a recent Type B meeting that a Phase IIb study of Androxal in men with secondary hypogonadism but naïve to testosterone treatment would provide a more solid data base for design of Phase III studies and eventual approval of such studies under a special protocol assessment. The agency further

stated that if the company moved into Phase III at this time it would do so at its own risk. Repros said the FDA accepted the notion of secondary hypogonadism associated with aging as an appropriate population and suggested that the next study involve men naïve to testosterone treatment or off testosterone treatment for at least six months. As outlined in the company's protocols, the FDA requested that the trial consist of four arms: placebo, two doses of Androxal and topical testosterone. Endpoints should consist of total testosterone and sperm counts at the end of the study compared to baseline. Repros said it agreed with the FDA's comments and noted it would analyze the previously completed ZA-003 study for the subset of men with morning testosterone less than 250 ng/dl and submit the data. Shares of Repros (NASDAQ:RPRX) fell 27 cents, or 17.8 percent, to close Tuesday at \$1.25.

• **Semafore Pharmaceuticals Inc.**, of Indianapolis, received orphan drug designation from the FDA for SF1126 in B-cell chronic lymphocytic leukemia. SF1126 is a peptidic prodrug of the PI3K and mTOR inhibitor LY294002 and is undergoing a Phase I trial.

• **Shire plc**, of Dublin, Ireland, announced that its wholly owned subsidiary Shire Holdings Luxembourg Sarl has acquired all of the issued shares and warrants of **Movetis NV**, of Turnhout, Belgium, and that shares in Movetis have been delisted from Euronext Brussels. Shire Holdings Luxembourg acquired 99.21 percent of the shares of Movetis on Oct. 12 following a successful tender offer launched in September. (See *BioWorld Today*, Aug. 4, 2010.)

• **Synageva BioPharma Corp.**, of Waltham, Mass., received orphan product designation from the European Medicines Agency for SBC-102 (recombinant human lysosomal acid lipase), an enzyme replacement therapy for lysosomal acid lipase deficiency. The drug previously received orphan drug status from the FDA.

Clinic Roundup

• The FDA approved an investigational new drug application from **Oxford BioMedica plc**, of Oxford, UK, for a Phase I/II trial of RetinoStat for wet age-related macular degeneration (AMD). RetinoStat is a gene therapy using the company's LentiVector gene delivery system. The trial will be carried out at the Wilmer Eye Institute at Johns Hopkins in Baltimore and will enroll 18 patients with wet AMD to evaluate three dose levels of the drug.

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