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PAGE 1 OF 8

Genmab Shares Dive Sharply on Zalutumumab Phase III Miss

By Cormac Sheridan
BioWorld Today Correspondent

Shares in Genmab A/S slid more than 20 percent Monday on news that zalutumumab, an antibody-targeting epidermal growth factor receptor (EGFR), failed to reach the primary endpoint of a pivotal Phase III trial in head and neck cancer.

The Copenhagen, Denmark-based company reported that patients who received the drug plus best supportive care attained a median survival of 6.7 months, while those on best supportive care alone attained a median overall survival of 5.2 months. However, the result was not statistically significant ($p = 0.0648$).

The drug did better on a secondary endpoint.

Patients in the drug treatment arm achieved a 61 percent increase in progression-free survival compared with

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Infection Deaths Halt Biogen, Roche Arthritis Drug Program

By Donna Young
Washington Editor

Biogen Idec Inc. and Roche AG have suspended development of ocrelizumab, an anti-CD20 monoclonal antibody, in rheumatoid arthritis after the firms' data safety monitoring board concluded that the risks of serious and opportunistic infections, some of which have been fatal, outweigh the drug's benefits.

Investors, however, took little notice, with shares of both firms barely budging Monday.

Shares of Cambridge, Mass.-based Biogen (NASDAQ:BII) closed at \$57.67, up 46 cents, while shares of Basel, Switzerland-based Roche (Swiss:RO) closed at CHF187 (US\$174.23), down CHF0.30.

The companies have yet to disclose the number and types of infections associated with ocrelizumab or divulge

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Imploding Combinatorial Explosion

Complex Interactions Simpler at Level of Individual Protein

By Anette Breindl
Science Editor

At the level of complex behaviors like cell death or proliferation, not to mention clinically, drug interactions can take a variety of forms: Two drugs may potentiate each other, leading to a synergistic effect that is more than the sum of its parts; they may be additive; or they may cancel each other. And predicting how two drugs will interact in a given case can be quite the headache. (See *BioWorld Today*, March 5, 2007.)

But a new study in the March 5, 2010, edition of *Cell* revealed "an unexpected level of simplicity in the way that proteins respond" to manipulation when the focus is on the levels of individual proteins, senior author Uri Alon told *BioWorld Today*—a simplicity that surprised him and his team.

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Financings Roundup

Chelsea Adds \$18M, Amended Droxidopa Study Nears Finish

By Jennifer Boggs
Assistant Managing Editor

A few months after Chelsea Therapeutics International Ltd. got a rare FDA blessing to modify the endpoints to an ongoing Phase III trial, the Charlotte, N.C.-based firm pulled in \$18.2 million in a registered direct offering led by Venrock.

Part of that funding will help finish up Study 301, a pivotal trial testing Northera (droxidopa) in neurogenic orthostatic hypotension (NOH), a condition characterized by unusually low drops in blood pressure as patients go from sitting or lying to standing.

That study had been under way last year when Chelsea reported that a higher-than-expected placebo response spoiled data from its first Phase III trial, Study 302, dropping its shares 61 percent and prompting the firm to

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U.S. PATENT DISCLOSURES

IntelGenx Corp., of Saint Laurent, Quebec, received a notice of allowance for a patent protecting CPI-300, a high-strength formulation of bupropion hydrochloride.

Intezyne, of Tampa, Fla., received a number of patents related to its IVECT method: U.S. Patent No. 7,638,558 covers polymeric micelles for drug delivery; U.S. Patent No. 7,601,796 covers synthesis of hybrid block copolymers and uses thereof; U.S. Patent No. 7,560,588 covers poly(ethylene glycol) containing chemically disparate endgroups; U.S. Patent No. 7,612,153 covers heterobifunctional poly(ethylene glycol) and uses thereof; and U.S. Patent No. 7,618,944 covers encapsulated amyloid-beta peptides.

MDRNA Inc., of Bothell, Wash., received a patent covering methods for the delivery of a broad array of compounds with pharmacological activity, including siRNAs, using targeting peptides that have preferential binding affinity for lung tissue.

Metabolon Inc., of Research Triangle Park, N.C., was awarded U.S. Patent No. 7,635,556, titled "Methods for Drug Discovery, Disease Treatment and Diagnosis Using Metabolomics." It's directed to identifying small molecules that are affected by a drug or toxin using metabolomics and provides a method to evaluate chemical agents for drugs effects and toxicity.

NanoBio Corp., of Ann Arbor, Mich., received a patent covering composition of matter claims for its lead anti-infective and vaccine product candidates.

NexBio Inc., of San Diego, received U.S. Patent No. 7,645,448, titled "Class of Therapeutics Protein-Based Molecules," which covers its sialidase pharmaceutical compositions, including lead compound DAS181 (Fludase) and methods of treating or preventing viral infection by influenza and parainfluenza.

Quality Management System Audits: Achieve Compliance

64 warning letters have been issued since January 2008 for noncompliance with CFR 820.22-quality system audits.

This, despite the tremendous scrutiny FDA investigators pay to internal audit procedures, and the importance of QS audits to the health of products that go out the door.

In this *BioWorld Today* audio conference, QS expert Susan Reilly will show you how to develop audits that prove compliance, increase efficiency and drive bottom line improvement. She'll describe how to organize and coordinate audits, from initial planning to team selection, to execution and documentation, through planning for the next audit.

Scheduled for Tuesday, March 16, 2010, 1-2:30 p.m. EST, registration is \$325. Call 1-800-688-2421 to register! Mention conference code **T10607**.

Stock Movers

03/08/10

<u>Company</u>	<u>Stock Change</u>
NASDAQ Biotechnology	-0.34%
BioNiche	+18.5%
Cell Therapeutics Inc.	+28.4%
Lexicon Pharmaceuticals Inc.	-10.7%
Nanosphere Inc.	+16.9%
Rosetta Genomics Ltd.	+17.2%

(Biotechs showing significant stock changes Monday)

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Genmab

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those in the comparator arm ($p = 0.0010$).

Widespread deviations from the trial protocol may have affected the final result.

The company said that 28 percent of patients in the comparator arm ($n = 95$) and 14 percent of those in the drug treatment arm ($n = 191$) received anticancer therapies that were not permitted by the protocol.

The median time to first use of other drugs was 79 days in the supportive care arm and 170 days in the zalutumumab arm.

"These additional treatments are likely the result of patients having very serious disease and short life expectancy," Genmab CEO Lisa Drakeman told analysts on a conference call.

The company will analyze the data and seek external advice before deciding on its next steps for the drug – if any. "Our immediate job is going to be to take a look at what the opinion leaders are going to have to say," Drake-man said.

Several cancer drugs gained approval in Europe on the basis of surrogate endpoints, she noted.

"We believe we have shown here that the drug is clinically active," said Genmab Chief Scientific Officer Jan van de Winkel.

Convincing the FDA of the drug's efficacy will be more

difficult, given its dislike of surrogate endpoints. Besides, Erbitux (cetuximab), another EGFR inhibitor, is already approved in the same indication. That drug is marketed by Bristol-Myers Squibb Co., of New York, and ImClone Systems Inc., a subsidiary of Eli Lilly and Co., of Indianapolis.

Analysts were skeptical about zalutumumab's prospects. "It hasn't a future," Lars Hatholt at Nordea Markets in Copenhagen told *BioWorld Today*. "The survival extension data weren't good enough."

"I don't think the company will be able to file with the current data," Gustaf Vahlne at SEB Enskilda in Stockholm, Sweden, told *BioWorld Today*. The company – or a partner – would need to perform a head-to-head study against Erbitux.

"That of course would be very time-consuming," Vahlne said. And the outcome would not be guaranteed. "I'm not sure if Genmab would like to take that risk," he said.

But there are still some outstanding questions that need answers. "We would like to see the per-protocol data," Vahlne said.

The company is funded through the next three years, assuming that it can raise a targeted DKK750 million (US\$137 million) from the disposal of a U.S. manufacturing facility in Brooklyn Park, Minn. Its financial guidance for the current year is not affected by the news.

Shares in Genmab (COPENHAGEN:GEN) closed Monday at DKK73.50, having closed on Friday at DKK92.35. ■

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Biogen

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how many study participants died from those infections.

Biogen revealed during its 2009 third-quarter earnings call in October that the FDA had placed the companies' Phase III FILM study of ocrelizumab in methotrexate-naïve rheumatoid arthritis patients on clinical hold. Also during that call, Biogen officials disclosed that the firms had halted their Phase III BELONG trial of ocrelizumab in lupus nephritis.

Roche said in an investor update in February that the serious and opportunistic infections tied to ocrelizumab plus the failure last year of its Phase III LUNAR study of Rituxan (rituximab) plus mycophenolate mofetil and corticosteroids in patients with lupus led to the discontinuation of the BELONG study.

"We concluded that the potential benefit does not outweigh the risks in this trial," Roche said in its presentation materials.

Biogen spokeswoman Amy Reilly told *BioWorld Today* that the future of ocrelizumab in rheumatoid arthritis currently is being evaluated by the companies.

"Patient safety is of the utmost importance in all of our drug development programs," Roche's Chief Medical Officer Hal Barron said in a statement.

Results from the FILM trial, in addition to results from another Phase III study of ocrelizumab in rheumatoid arthritis, known as SCRIPT, remain blinded, with data expected to be read out by June.

Just this past December, the companies reported that their international, randomized, multicenter, three-arm, parallel-group Phase III STAGE study of ocrelizumab in combination with methotrexate met its primary endpoint of improving signs and symptoms of rheumatoid arthritis in patients who had an inadequate response to methotrexate at weeks 24 and 48. (See *BioWorld Today*, Dec. 14, 2009.)

Patients in the STAGE study received two courses at six-month intervals of either one of two dosages of ocrelizumab or placebo by intravenous infusion on day one and day 15, with weekly methotrexate as a background therapy.

Roche and Biogen plan to present more details of the STAGE study at an upcoming medical meeting, Reilly said.

While the companies have experienced setbacks in rheumatoid arthritis and lupus with ocrelizumab, their multicenter, randomized, parallel-group, partially-blinded placebo- and interferon beta-1a-controlled, dose-finding Phase II trial in relapsing, remitting multiple sclerosis (RRMS) met its primary endpoint.

Biogen and Roche in December reported that the RRMS Phase II study, which is ongoing, showed that ocrelizumab had a strong effect with a highly statistically significant reduction in signs of disease activity measured by brain lesions vs. placebo in 220 treatment-naïve and previously treated patients, Reilly noted. Biogen and Roche plan to also present details from the RRMS study at an upcoming medical meeting, she said.

In the RRMS trial, which is evaluating the efficacy and safety of ocrelizumab at 600-mg and 2-g dosages, patients were treated for 24 weeks, with assessments at four-weekly intervals to measure brain lesions via MRI scans.

The primary endpoint of the study was efficacy measured by gadolinium-enhancing T1 lesions observed by MRI scans of the brain at weeks 12, 16, 20 and 24 compared with placebo.

The secondary endpoints of the study included annualized relapse rate at week 24, total number of new gadolinium-enhancing T1 lesions at four-weekly intervals, safety and tolerability of two dose regimens compared to placebo and interferon beta-1a and overall safety of ocrelizumab for up to 96 weeks.

During Biogen's 2009 fourth-quarter earnings call last month, CEO James Mullen characterized the RRMS study as "certainly interesting" and "worthy to continue to progress the trial in to Phase III."

"The specifics of that program are yet to be determined with our partner," Mullen said last month.

South San Francisco-based Genentech Inc., now a subsidiary of Roche, and Biogen first entered into a collaboration agreement in 1995 to develop and co-market Rituxan, which currently is approved for certain types of lymphoma, leukemia and moderate-to-severely active rheumatoid arthritis.

The companies in 2003 amended that agreement to cover development and commercialization of certain next-generation anti-CD20 products, including ocrelizumab, said Genentech spokeswoman Nikki Levy. ■

OTHER NEWS TO NOTE

• **Acetylon Pharmaceuticals Inc.**, of Boston, exclusively licensed rights to a platform technology and chemical methodology for conducting high-throughput screening and lead optimization for histone deacetylase inhibitor compounds, as well as portfolio of small-molecule selective HDACs, from Harvard University and the Dana-Farber Cancer Institute. The license includes rights to the first selective inhibitor of HDAC6. Financial terms were not disclosed.

• **Acologix Inc.**, of Hayward, Calif., said preclinical results demonstrated AC-100, which is derived from an endogenous human protein, promotes cartilage regeneration in goats with standardized defects in knee cartilage. In the study, four weekly intra-articular injections of AC-100 or placebo were administered, and quantity and quality of cartilage regeneration were evaluated after six months. AC-100 dose dependently promoted cartilage repair compared with placebo, and the new cartilage formed in response to AC-100 was mature, normal hyaline cartilage as assessed by several histological staining methods, the company said. AC-100 also exhibited a favorable safety profile, with no inflammatory response.

Proteins

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Alon is professor with a joint appointment in molecular and cell biology and the physics of complex systems at the Israeli Weizmann Institute of Science. "As physicists, we are culturally prepared for at least having the hope that there will be simplicity" at the heart of complex observations, he said. Nevertheless, Alon added, he and his team were initially "floored" by the findings reported in *Cell*.

Alon and his colleagues showed that when using cellular protein levels as a readout, one type of interaction predominates. With few exceptions, "Protein dynamics in response to combinations of drugs are described by a linear superposition (weighted sum) of their response to individual drugs."

Furthermore, combinations of three or four drugs could be predicted quite well from knowing the responses to two-drug combinations – a finding that suggested it may be possible to predict the effects of multidrug combinations without having to slog through exponential increase in experiments that would be necessary to test them.

In their work, the authors used a so-called dynamic proteomics approach: Using fluorescent labeling, they studied 15 different proteins involved in different aspects of cellular functioning – including oxidative stress, DNA repair, metabolism and apoptosis. The team first exposed cells to 13 different drugs and tracked the changes in protein concentrations.

Then, they tested two-drug combinations – and found that in most cases, protein levels responded to two-drug combinations in a way that was a weighted average of their response to one drug. That is, if both drugs individually increased the level of protein, their combination also would increase the protein level, and the response to the combination would be between the response to the two drugs individually, though not necessarily midway between the two. The scientists also tested three- and four-drug combinations and found that they could predict protein responses to cocktails from their respective two-drug combinations.

One important exception, especially from a drug discovery point of view, was the PI3 kinase inhibitor wortmannin; combinations of wortmannin and other drugs did not sum up to a linear average. Alon said his team at this point has no good explanation for what makes PI3K different. "I wish I knew" he said.

Likewise, when asked how the simplicity his team has demonstrated at the protein level turns into the complexity of effects that can be seen at the cellular and clinical levels, Alon cheerfully admitted he is "stumped," then showed his physicist roots. "I actually haven't given up on the possibility of simplicity" at more complex levels, either, though unearthing such simplicity will obviously take a breakthrough in perspective.

Alon and his team are currently testing more cell lines, proteins and drugs to see how far the effect extends, as well as probing whether protein level changes are also

unexpectedly simple in response to "nondrug perturbations" such as viral infections.

The work suggested that predicting drug combinations may turn out to be a smaller-than-expected hurdle to the development of drug combinations. Most people agree that treating complex diseases successfully will take drug combinations. But testing the effects of drug combinations suffers from combinatorial explosion, or the fact that the number of possible combinations increases exponentially with the number of drugs. That is, two drugs can be given in one possible combination; three drugs can be given in three possible combinations; four drugs can be given in 11 possible combinations; and the math gets worse from there, especially once different doses are in the mix. If higher-order combinations can indeed be predicted from two-way combinations, the number of experiments required to test them would turn out to be much more manageable than is currently feared.

At a much deeper and more long-term level, the findings suggested that it may be possible to develop drugs that have different goals than presently. Rather than trying to, for example, kill cancer cells, future physicians might have an array of drug at their disposal, each of which influences that the level of one particular protein in a cell. With a large arsenal and a deep understanding of how each individual protein contributes to disease, it might be possible to come up with custom drug cocktails that "push cells from the sick state to the healthy state," Alon said.

"It may take the whole century to get there," he added. "But that's the vision." ■

OTHER NEWS TO NOTE

• **Entest BioMedical Inc.**, of San Diego, said it created three bone marrow-derived stem cell lines useful for optimizing laser intensities and wavelengths in laser-enhanced stem cell therapy, which the company said would assist in the progress of its therapy for chronic obstructive pulmonary disease. Entest said ENT-CL101, ENT-CL221 and ENT-CL303 are similar in nature to mesenchymal stem cells, stable in cell culture and can be expanded en masse for wide-scale screening.

• **Enzon Pharmaceuticals Inc.**, of Bridgewater, N.J., said that it reduced its debt by \$116 million during the period in which it sold its specialty pharmaceutical business. As a result of the Jan. 29 sale, the company was required to offer to repurchase for cash its convertible notes at face value. The sale of the specialty pharmaceutical business also triggered an increase in the conversion rate to 116.535 shares per \$1,000 principal amount during the period Jan. 29 to March 4. The enhanced conversion period has expired, and the original conversion rate of 104.712 shares per \$1,000 principal amount of notes is again in effect.

Financings Roundup

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rethink its trial design for droxidopa, a synthetic precursor of norepinephrine. (See *BioWorld Today*, Sept. 25, 2009.)

Chelsea maintained that the drug showed clear clinical benefit, even though it fell short of statistical significance. And, given the fact that droxidopa has been marketed in Japan since 1989, the company believed a reworked trial design might yield a better outcome. But that meant convincing the FDA to allow a change in protocol midway through a pivotal trial.

"We had a couple of things working to our advantage," Chelsea spokeswoman Kathryn McNeil told *BioWorld Today*. For one, NOH is still a rare disease, so "there's a much narrower body of clinical research" at hand to help design studies, especially when it comes to demonstrating symptomatic improvement in NOH patients.

The only available therapy in NOH is midodrine, which gained approval using blood pressure measurement as the primary endpoint, but the drug's postmarketing requirement was to show in clinical testing an improvement in NOH symptoms and "nobody's been able to do that," McNeil said.

Midodrine, which has since gone generic, also is limited by its side-effect profile and carries a black-box warning.

But data from droxidopa's earlier Phase III study might have been the most persuading factor for Chelsea.

"When we presented data to the FDA, they saw there was such broad evidence of efficacy" and agreed that the original endpoint was not sufficient to capture the symptomatic benefit, McNeil said.

The failed Study 302 had used a single question from the orthostatic hypotension symptom assessment (OHSA) score – dizziness – to measure droxidopa's effect. The amended protocol for Study 301 employs a more comprehensive measurement, defined as the mean change in the Orthostatic Hypotension Questionnaire composite score between the droxidopa and placebo arms.

The FDA also agreed to let Chelsea enroll an additional 24 patients, increasing the power of the trial by greater than 80 percent. Enrollment is expected to be completed in the second quarter, with top-line data coming in the third quarter.

Two successful trials likely will be needed for a new drug application, so Chelsea plans to start a confirmatory study next quarter. That trial, designated Study 306, will be a little different, enrolling specifically Parkinson's patients with NOH and will test droxidopa treatment over a slightly longer duration, McNeil said.

Data from Study 306 are anticipated in the second quarter of 2011.

The company, which reported a net loss of \$7.1 million, or 22 cents per share, for the third quarter of 2009, expected to end the year with about \$20 million in cash,

enough to fund operations into the third quarter of 2010. The latest financing should get Chelsea into 2011.

Terms of the latest financing called for Chelsea to offer 6.7 million shares priced at \$2.72 apiece, plus warrants for about 2.3 million shares.

Net proceeds totaled about \$16.8 million. In addition to its droxidopa program, the company plans to use funds for a Phase II trial of antifolate compound CH-4501 in rheumatoid arthritis and for general corporate purposes.

Leerink Swann served as lead placement agent, with Needham & Co. LLC acting as co-placement agent.

Shares of Chelsea (NASDAQ:CHTP) closed at \$2.94 Monday, up 6 cents.

In other financings news:

- **Genta Inc.**, of Berkeley Heights, N.J., is raising \$25 million in gross proceeds in a private placement of convertible notes, expected to close on or about March 10. Funds will be used to ensure adequate follow-up to determine overall survival results from the company's recently completed Phase III trial of Genasense (oblimersen sodium) plus chemotherapy in first-line advanced melanoma patients and to accelerate development of other pipeline products.

- **Lexicon Pharmaceuticals Inc.**, of The Woodlands, Texas, is planning to raise \$95 million in a stock sale, though it has not yet announced the number of shares to be offered or share price. Lexicon also intends to grant underwriters a \$14.25 million overallotment option. Based on a March 5 closing stock price of \$1.78, the company anticipates net proceeds of about \$89.4 million – or \$153.6 million if shareholder Invus exercises its pro rata right and underwriters exercise overallotment options in full. The money will be used to fund R&D work. Morgan Stanley & Co. Inc. and J.P. Morgan Securities Inc. will be acting as joint bookrunners, with Cowen and Co. LLC and Thomas Weisel Partners LLC acting as co-managers. Shares of Lexicon (NASDAQ:LXRX) closed at \$1.59 Monday, down 19 cents.

- **MabCure Inc.**, of Hasselt, Belgium, completed a \$1 million private placement, comprising a \$500,000 cash investment and the conversion of a \$500,000 bridge loan that was made in September 2009. Under the terms, MabCure will issue 2 million units – each consisting of one share of common stock, one two-year nontransferable common stock purchase warrant exercisable at a price of 60 cents per share and one two-year nontransferable common stock purchase warrant exercisable at a price of 70 cents per share. Each unit is priced at 50 cents. MabCure will use the funds to pursue clinical trials in Europe and Asia to test its anti-ovarian MAb in diagnosing ovarian cancer in the blood and urine of patients suspected of having the disease.

- **Omthera Pharmaceuticals Inc.**, of New York, closed a \$6.5 million Series A round led by Sofinnova Part-

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Financings Roundup

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ners. Funds will be used to advance Epanova, an omega 3 fatty acid containing a formulation of eicosapentaenoic acid and docosahexaenoic acid, which has shown promising results in lowering triglycerides in early clinical trials. Omthera plans to start comparative bioavailability trials in the middle of this year, with Phase III testing expected to start in patients with severe hypertriglyceridemia in late 2010 or early 2011.

- **Response Genetics Inc.**, of Los Angeles, entered a purchase agreement with new and existing investors and certain funds managed by Lansdowne Partners LP to raise about \$4 million in a private placement of about 3 million

shares priced at \$1.31 each. The firm develops molecular diagnostic tests for cancer. Shares of Response Genetics (NASDAQ:RGDX) closed Monday at \$1.22, up 2 cents.

- **YM BioSciences Inc.**, of Mississauga, Ontario, increased its recent registered direct offering from \$15 million to about \$17.5 million. The company is offering units – each consisting of one common share and one half of one common share – priced at \$1.20 per unit. Funds will be used to support drug development activities and for general corporate purposes. Roth Capital Partners LLC served as lead placement agent, with Bloom Burton & Co. Inc., Griffin Securities Inc. and Haywood Securities Inc. acting as co-placement agents. Shares of YM (AMEX:YMI) closed at \$1.15, up 1 cent. ■

OTHER NEWS TO NOTE

- **ExonHit Therapeutics SA**, of Paris, and **bio-Mérieux**, of Marcy L'Etoile, France, have decided not to pursue their collaboration in colon cancer, following a recent review of data by their scientific committee. Both companies continue to collaborate in the field of prostate cancer.

- **Isis Pharmaceuticals Inc.**, of Carlsbad, Calif., earned a \$6 million milestone payment from **Bristol-Myers Squibb Co.**, of New York, related to the acceptance of initial regulatory filings to begin Phase I studies for BMS-PCSK9Rx. The drug candidate is an antisense drug that arose out of the ongoing collaboration between Bristol-Myers and Isis to identify antisense drugs targeting PCSK9 to lower low-density lipoprotein (LDL) cholesterol.

- **Nabi Biopharmaceuticals Inc.**, of Rockville, Md., closed its option and license agreement for NicVAX (nico-

tine conjugate vaccine), dated Nov 13, 2009, with **Glaxo-SmithKline Biologicals SA**, of Rixensart, Belgium. As a result, Nabi is entitled to receive an up-front payment of \$40 million and GSK has been granted an option to exclusively in-license NicVAX on a worldwide basis and a license to develop next-generation nicotine vaccines using Nabi's intellectual property. In addition, Nabi is eligible to receive up to \$460 million in potential option fees and regulatory, development and sales milestones for NicVAX and follow-on nicotine vaccines. Nabi also will receive royalties on global sales of NicVAX should GSK exercise its option, as well as royalties on global sales of next-generation nicotine vaccines developed by GSK based on intellectual property licensed from Nabi.

- **Ricerca Biosciences LLC**, of Concord, Ohio, said it finalized its acquisition of the discovery and preclinical business of **MDS Pharma Services**, of King of Prussia, Pa., which has facilities and almost 600 associates in Bothell, Wash.; Lyon, France; and Taipei, Taiwan.

CLINIC ROUNDUP

- **Action Pharma A/S**, of Holte, Denmark, has completed a proof-of-concept Phase IB study with API030 for treatment of Type II diabetes associated with obesity. API030 administered orally once daily for two weeks in obese human volunteers significantly improved glucose metabolism. API030 was well tolerated and did not increase blood pressure

- **Argos Therapeutics**, of Durham, N.C., announced positive data from a Phase II trial that evaluated the safety, clinical response and immune response of AGS-003 in newly diagnosed patients with metastatic renal cell carcinoma. Data showed AGS-003 induced a tumor-specific immune response, performed better than interferon-alpha on a measure of progression-free survival and was well tolerated, the firm said. The results serve as preliminary proof of concept for the compound, showing the

immunotherapy can induce an immune response to the very patient-specific tumor antigens that are targeted, it added. The data were presented at the American Society of Clinical Oncology Genitourinary Cancers Symposium in San Francisco.

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CLINIC ROUNDUP

• **AstraZeneca plc**, of London, said its Phase II/III trial comparing VEGF inhibitor Recentin (cediranib) to Avastin (bevacizumab, Genentech Inc./Roche AG) in first-line metastatic colorectal cancer showed no statistically significant difference between the two drugs, but failed to establish the noninferiority of Recentin in progression-free survival. The trial will continue as overall survival data are collected, and a second ongoing pivotal trial is comparing Recentin plus chemotherapy to chemotherapy alone.

• **Harbor BioSciences Inc.**, of San Diego, reported encouraging data from its ongoing Phase I/IIa trial with Apoptone (HE3235) for castration-resistant prostate cancer. To date, 42 taxane-resistant prostate cancer patients have been entered into the clinical trial at seven dose levels. Of those, 28 (67 percent) reached their first reassessment (two 28-day cycles), 15 (56 percent) of those had stable disease on scans or imaging and have received one to eight additional treatment cycles before disease progression. Six patients continue to receive treatment. The Kaplan-Meier estimate for the median time to progression is 15.3 weeks for the trial. Due to early signs of activity, the 20-mg dose group was expanded to include 14, of whom 11 were evaluable with an actual median time to progression of 20 weeks. The data were presented at the American Society of Clinical Oncology Genitourinary Cancers Symposium in San Francisco.

• **Millennium**, of Cambridge, Mass., a unit of Takeda Pharmaceutical Co. Ltd., reported data from the Phase I portion of a Phase I/II study of TAK-700 an oral, nonsteroidal androgen synthesis inhibitor of the 17,20 lyase, in metastatic, castration-resistant prostate cancer. Of 26 previously treated patients, all 15 who received TAK-700 orally twice daily for three or more cycles experienced a decrease in prostate-specific antigen levels, and within that patient group, there was a decrease in testosterone to extremely low concentrations. Twenty-three of 26 patients experienced at least one drug-related treatment-emergent adverse event, and the most common were fatigue, nausea, constipation, anorexia and vomiting. Data were presented at the American Society of Clinical Oncology's Genitourinary Cancers Symposium in San Francisco. The Phase II portion of the study is ongoing, and planning for Phase III studies is under way.

• **Nektar Therapeutics Inc.**, of San Carlos, Calif., reported initial progression-free survival data from its ongoing Phase II trial of monotherapy NKTR-102 for platinum-resistant ovarian cancer. While standard PFS in these patients is 9.1 weeks to 13.6 weeks, women receiving NKTR-102 every 14 days or every 21 days had PFS of 12.2 weeks and 21 weeks, respectively. Full data are expected

later this year. NKTR-102 is a topoisomerase I inhibitor-polymer conjugate.

• **NeuroSearch A/S**, of Ballerup, Denmark, said additional data from the Phase III trial of Huntexil (pridopidine) for Huntington's disease showed the drug slowed disease progression in certain patients. NeuroSearch previously said twice-daily Huntexil treatment met the study's primary goal of improving voluntary motor function, although once-daily treatment did not. Detailed data have not been disclosed. (See *BioWorld Today*, Feb. 4, 2010.)

• **Novavax Inc.**, of Rockville, Md., completed enrollment of 4,500 patients in a pivotal study of its virus-like-particle vaccine for 2009 H1N1 pandemic influenza. Enrollment was completed in less than five months, and positive data will position the vaccine for approval in Mexico.



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- Address assay challenges for a PEGylated biotherapeutic
- Overcome challenges associated with tolerance induction in preclinical and clinical studies
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