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AVEO, Astellas Seek to Hang Tivozanib Hat on PFS Data

By Marie Powers
Staff Writer

AVEO Pharmaceuticals Inc. and partner Astellas Pharma Inc. reported top-line data from the global, randomized Phase III TIVO-1 trial indicating that lead compound tivozanib demonstrated superiority over Nexavar (sorafenib, Onyx) in advanced renal cell carcinoma (RCC), meeting the primary endpoint of progression-free survival (PFS).

TIVO-1 is the first registration study comparing an investigational agent – in this case, an oral, once-daily, investigational tyrosine kinase inhibitor – against an approved VEGF therapy in first-line RCC.

Cambridge, Mass.-based AVEO offered an upbeat assessment of the data. The 517 patients enrolled in TIVO-1 had clear cell RCC, had undergone a prior nephrectomy and had not previously been treated with either a VEGF or mTOR therapy. Based on the top-line analysis of events in TIVO-1 as

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Fun with Finances

Biotech Rings in 2012 With A Toast to 2011 VC Tallies

By Cynthia Robbins-Roth
***BioWorld Today* Columnist**

It was another heart attack-inducing year for biotech fans, with the market gyrations approaching the speed of light.

We did end on a positive trend, with venture investing posting a 15 percent gain by year-end, after lagging behind 2010's numbers for much of 2011.

The big total brought in by U.S. biotech venture rounds in 2011 was $2.3 billion, a nice nudge up from last year's $2 billion. (See the charts on p. 4)

Even nicer was that investors showed a big bump-up in enthusiasm for investing in young companies; 37 companies raised $665 million in their Series A rounds, a 39 percent increase over 2010's haul. Last year, the Series A class poured $479 million into 41 companies,

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How Miravirsen Does it?

New Insight into Hepatitis C Virus Cofactor MiRNA-122

By Anette Breindl
Science Editor

Researchers from the University of North Carolina at Chapel Hill have gained new insights into why the hepatitis C virus needs the microRNA miR-122 as a partner in crime – and in doing so, have described a new general mechanism by which miRNAs can act on their targets to affect gene expression.

"We have known since 2005 that [miR-122] is a required host factor" for hepatitis C infection – and that knowledge is now being applied in several clinical trials, Stanley Lemon told *BioWorld Today*. "But what it does has been a mystery."

The novel mechanism – the stabilization of mRNA by microRNA – is most likely restricted to "a small subset" of miRNAs, he added. "But I would be very surprised if this turned out to be unique. Lemon is professor of medicine

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Washington Roundup

Biosimilar Path Expected to Be Under Construction for Years

By Mari Serebrov
Washington Editor

WASHINGTON – The Congressional Research Service (CRS) has a few words for those hoping to use the new biosimilar pathway as a shortcut to cash in quickly on the high price of biologics. Be patient. And watch out. This new road could be under construction for a long time.

In a recent report on follow-on biologics law and intellectual property rights, the CRS predicted that scientific and legal issues could be road hazards that will likely keep the FDA and the courts busy for many years.

Likewise, it also may take some time for the biologics industry "to develop a working familiarity and appropriate strategies within the BPCIA [Biologics Price Competition and Innovation Act] framework," the report said. "As a result, marketplace availability of significant numbers of

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INSIDE:

Financings Roundup

• **Advaxis Inc.**, of Princeton, N.J., said it entered a convertible notes purchase agreement with certain investors for the purchase of the aggregate principal value of about $1.2 million on convertible promissory notes for an aggregate purchase price of about $1 million. Funds are expected to help support progress of the firm's cervical cancer trials in India and a U.S. trial in human papillomavirus-associated disease. Rodman & Renshaw LLC acted as exclusive placement agent.

• **Amsterdam Molecular Therapeutics BV**, of Amsterdam, the Netherlands, said it raised €2.5 million (US$3.3 million) in a private placement to three existing shareholders: Forbion Capital Partners, Gilde Healthcare Partners and Advent Venture Partners. Under the terms, AMT agreed to issue about 7.4 million shares priced at €0.34, with proceeds aimed at providing additional flexibility for exploring strategic options.

• **Bionovo Inc.**, of Emeryville, Calif., said it entered a $5 million securities purchase agreement with Socius CG II Ltd., a Bermuda-based subsidiary of Socius Capital Group LLC. Under the terms, the company has the right, at its discretion, to sell to Socius up to a total of $5 million of redeemable Series A preferred stock, payable in tranches, over a two-year period. Bionovo is working on drugs in the areas of women's health and cancer.

• **Elite Pharmaceuticals Inc.**, of Northvale, N.J., said it entered a securities purchase agreement with Socius CG II Ltd., a subsidiary of Socius Capital Group, to sell up to $5 million of nonconvertible Series F preferred stock to Socius over a two-year period. Proceeds will be used for product development, including the scale-up of products using Elite's abuse-deterrent technology, as well as for other corporate purposes.

• **Galecto Biotech AB**, of Lund, Sweden, was formed with support from Novo A/S, Merck Serono Ventures and Forskarpatent in an undisclosed seed round. The company will develop modulators of galectins, initially focusing on galectin 3 inhibitors, which have demonstrated potential in a range of debilitating diseases such as fibrosis.

Coming Thursday in *BioWorld Perspectives:*

The Good, the Bad and . . . the Huh?
A 2011 Biotech Recap

As we head into 2012 (and possibly an apocalyptic countdown, if those Mayans are to be believed), let's take a look back at some of the highs and lows of the biotech industry in 2011.

For more on this topic, see tomorrow's edition of *BioWorld Perspectives*, an op-ed e-zine that provides fresh commentary from the *BioWorld Perspectives* blog, http://bioworld.blogs.bioworld.com. Plus, you'll have access to free articles from *BioWorld Today*, *BioWorld International* and *BioWorld Insight*.

If you don't already receive this complimentary e-zine, **visit bioworld.com to opt in.**

Stock Movers

1/3/12

Company	Stock Change	
Nasdaq Biotechnology	+$9.99	+0.92%
Alexza Pharmaceuticals Inc.	+$0.12	+14.29%
AVEO Pharmaceuticals Inc.	-$3.37	-19.59%
EntreMed Inc.	+$0.20	+21.05%
Tengion Inc.	+$0.10	+21.28%
Vermillion Inc.	+$0.28	+23.93%

(Biotechs showing significant stock changes Tuesday)

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AVEO

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determined by a blinded, independent review committee, tivozanib demonstrated a statistically significant improvement in PFS, with a median PFS of 11.9 months compared to a median PFS of 9.1 months for sorafenib in the overall study population, according to the company.

In treatment-naïve patients, who represented approximately 70 percent of the study population, the difference was more pronounced, with tivozanib demonstrating a median PFS of 12.7 months compared to a median PFS of 9.1 months for sorafenib.

In addition, AVEO said tivozanib was well tolerated, consistent with its Phase II experience, with hypertension the most commonly reported side effect. The company did not disclose details of the safety findings.

Based on the findings, AVEO and Astellas, of Tokyo, said they plan to submit a single core dossier for marketing approval of tivozanib in the U.S. and Europe this year, subject to final analysis of complete trial data.

The next step is a pre-new drug approval meeting with regulatory authorities to determine what data to include in the parallel submissions, according to Tuan Ha-Ngoc, AVEO's president and CEO. "At that time, we'll have a more definitive idea of when exactly in 2012 we'll be in a position to make the submissions on both sides of the ocean," he said.

"There can never be any better New Year's present," Ha-Ngoc told *BioWorld Today*.

Investors didn't share the company's optimism, however. AVEO shares (NASDAQ:AVEO) fell $3.37 Tuesday, or 19.6 percent, on 14 times average volume even as the broader market was posting hefty gains. The stock closed at $13.83, near the bottom of its 52-week range.

While declining to comment on the stock movement, Ha-Ngoc vigorously defended the study results, which were reported as the company nears its 10-year anniversary. In addition to showing statistically meaningful superiority to Nexavar and meeting endpoints that address unmet medical need, the compound also demonstrated a good safety profile, delivering "a solid foundation on which we can start delivering, first, tivozanib and then the rest of our pipeline," he said.

"Sometimes people focus only on efficacy, and of course for cancer that is foremost in the mind of patients and physicians," he added. "But the safety part is very important. If you cannot tolerate the drug, you have to get off the treatment. What good is a drug with nine, 10, 11 or 12 months of PFS if, by month six, you have to get out of treatment?"

On top of that, cancer patients are seeking drugs that allow them "to have as normal a life as possible" during treatment, Ha-Ngoc said, adding that many currently suffer as much from their therapy as from the disease itself. In both of those respects, tivozanib will prove superior in RCC, he maintained.

Although the FDA has keyed on overall survival data in recent years when reviewing cancer compounds, Ha-Ngoc said the company received assurances from regulatory agencies during its post-Phase II meetings that PFS will be accepted as the standard for approval in first-line RCC.

"Once the patient progresses on first-line, the patient will go on to additional second- or sometimes third- or fourth-line therapies, and the survival data will be so confounded that you cannot draw any conclusions," he explained.

In addition, last month FDA officials publicly stated at an ODAC meeting that they would accept PFS as the endpoint for RCC, "which gives us an additional level of timely assurance," Ha-Ngoc said.

Study participants continue to be observed to gather additional data for further analyses, with detailed findings from TIVO-1 scheduled for presentation at the American Society of Clinical Oncology's annual meeting in June.

Although AVEO raised more than $100 million last June in an underwritten public offering and has built an infrastructure to launch tivozanib, the drug must succeed commercially for AVEO to fully leverage its partnership with Astellas, which calls for up to $1.3 billion in milestones. (See *BioWorld Today*, Feb. 17, 2011, and June 16, 2011.)

The global agreement includes the application of tivozanib to a broad range of cancers, with AVEO leading commercialization in North America and Astellas leading commercialization in the European Union. AVEO and Astellas are evaluating the compound in colorectal cancer and plan to launch a study in breast cancer this year.

In a flash update, Canaccord Genuity analyst George Farmer suggested AVEO might have to rely on its partner's clout to propel the compound's commercial success.

"Along with safety data, we believe the Street will also be looking for tivozanib performance in cytokine-experienced patients, which constituted about 30 percent of the TIVO-1 treatment population," Farmer wrote. "While all data so far suggest that tivozanib is superior to standard-of-care Sutent [sunitinib, Pfizer Inc.] for treatment of RCC, we see a challenging marketing battle ahead with axitinib [Inlyta, Pfizer Inc.], which we expect will win approval as second-line treatment by the April 29 PDUFA date, but will be used off-label in front-line disease. Muscle from marketing partner Astellas will be essential for tivozanib market position, in our view." ■

VC

Continued from page 1

with a median deal size of $20 million. Investors were more generous with this year's median deal size of $50 million.

Investors showed the same basic support for clinical-stage deals over the two-year period, but shoveled a greater percentage of their cash into early stage specialty pharmaceutical this year.

The Series B rounds for both years funded raised similar amounts: $750 million this year vs. $763 million in 2010 for almost the same number of deals (36 vs. 37). The differences were seen in the increased interest this year in clinical-stage investments (65 percent of the dollars, vs. 44 percent in 2010) and specialty pharmaceuticals (46 percent of the dollars, vs. 22 percent in 2010).

The more mature private companies (Series C and higher) brought in a comfortable $862 million this year, an 8 percent increase over 2010. The emphasis on clinical-stage deals and lack of interest in specialty pharma stayed steady from 2010 to 2011.

But can anyone get liquidity?

Well, not so much. The number of companies making it public this year dropped to six, raising a paltry $375 million: a 33 percent drop from 2010's pathetic $561 million haul for only nine companies. All of this year's initial public offerings (IPO) had products in the clinic or on the market, and 63 percent of the dollars went into specialty pharma companies.

However, we are still light years beyond the down-right scary $5.8 million IPO haul in 2008 and the two-deal/$158 million IPO class of 2009.

So let's agree to be optimistic – the line is trending up!

Good luck in 2012, and have fun in San Francisco at the JP Morgan Healthcare conference. ■

Jan.-Dec. 2011 Venture Investing

Total Raised = $2.3B

	Series A	Series B	Higher Rounds
Total raised	$664.8M	$749.6M	$861.7M
Deals	37*	36**	24***
Median Deal	$50.5M	$51M	$51M
Range	$1M to $100M	$0.5M to $102M	$1.5M to $100M
Clinical Stage	17%	65%	70%
Specialty Pharm	42%	46%	10%

*** 6 in Phase I, 4 in Phase II**
**** 7 in Phase I, 8 in Phase II, 2 in Phase III**
***** 8 in Phase I, 6 in Phase II, 5 in Phase III**

2011 IPOs: Total $375.8M raised. Total deals = 6, 100% in clinic, 63% specialty pharma.
All data: BioWorld Snapshots

Jan.-Dec. 2010 Venture Investing

Total Raised = $2B

	Series A	Series B	Higher Rounds
Total raised	$479M	$763M	$795M
Deals	41*	37**	33***
Median Deal	$20M	$29M	$41.5M
Range	$0.25M to $40M	$6M to $51M	$5M to $78M
Clinical Stage	20%	44%	85%
Specialty Pharm	29%	22%	20%

*** 6 in Phase I, 3 in Phase II**
**** 5 in Phase I, 11 in Phase II, 1 in Phase III**
***** 7 in Phase I, 15 in Phase II, 1 in Phase III, 3 on market**

2010 IPOs: Total $560.8M raised. Total deals = 9, 100% in clinic, 16% specialty pharma.
All data: BioWorld Snapshots

U.S. Patent Disclosures

• **RegeneRx Biopharmaceuticals Inc.**, of Rockville, Md., received a notice of allowance for a patent with claims directed to compositions for topical administration of Thymosin beta 4 to skin and methods for improving or treating damage to skin, including from radiation or scar tissue, and methods of regenerating or revitalizing skin tissue.

• **Resverlogix Corp.**, of Calgary, Alberta, received U.S. Patent No. 8,053,440, which contains composition-of-matter claims for lead molecule RVX-208 and structurally related compounds.

• **Revotar Biopharmaceuticals AG**, of Berlin, received U.S. Patent No. 8,039,601, titled "Crystalline Forms of 1,6-Bis [3-(3-carboxymethylphenyl)-4-(2-alpha-D-mannopyranosyloxy)-phenyl] hexane." It covers a new polymorph form of the pan-selectin antagonist and pharmaceutical compositions for Revotar's product for chronic obstructive pulmonary disorder and other respiratory diseases.

• **Rexahn Pharmaceuticals Inc.**, of Rockville, Md., received U.S. Patent No. 8,034,829, titled "5, 6, or 7-Substituted-3-(hetero) arylisoquinolinamine derivatives and therapeutic use therof." It covers several new isoquinolinamine compounds and their pharmaceutical composition and method for producing an antitumor effect.

Hepatitis

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at the University of North Carolina at Chapel Hill and the senior author of the study, which appeared in the Jan. 2, 2012 online edition of the *Proceedings of the National Academy of Sciences*.

MicroRNAs typically decrease the expression of the mRNAs they target. They bind to one end of their target – the 3' untranslated region – and recruit a miRNA-induced silencing complex, or RISC, which destabilizes the microRNA.

But miR-122's effects on hepatitis C genome, which is made of RNA rather than DNA, are exactly the opposite.

In their work, Lemon and his team showed that miR-122 binds to the 5'-end of hepatitis RNA. Once there, it recruits a protein complex that looks to be similar in some respects to the RISC. Like RISC, this complex contains an argonaute protein.

But this particular complex stabilizes the hepatitis C RNA – most likely by protecting it from an enzyme, a 5'-exonuclease, that would normally degrade it, though Lemon said that remained to be demonstrated experimentally.

His team plans to follow up their current results by investigating the contents of the complex in more detail, to see whether that exonuclease is the major way in which hepatitis C virus meets its end in cells.

Lemon said it is a surprisingly unplowed area in science. Though there is a very large body of experimental work looking at how cellular RNA decays and how that affects gene expression levels, "very few people have spent much time thinking about the decay of viral RNA."

The findings explained, on a molecular level, why miR-122 targeting has shown clinical promise for treating hepatitis C.

Hepatitis C is a major viral scourge, affecting an estimated 170 million people worldwide. Treatment options increased dramatically in 2010 with the approval of Vertex Pharmaceuticals Inc.'s Incivek (telaprevir) and Merck & Co. Inc.'s Victrelis (boceprevir), but there's definitely room for improvement.

And some of that improvement could conceivably come from targeting miR-122, which makes up over half of all mature miRNAs in the liver and is necessary for HCV to replicate.

Regulus Therapeutics Inc. is developing a miR-122 targeted anti-miR with partner GlaxoSmithKline plc. And Danish Biopharma company Santaris A/S is in the clinic with its miR-122 antagonist miravirsen.

Last November, the company presented results from a Phase IIa trial at the annual meeting of the American Association for the Study of Liver Diseases showing that four weeks of miravirsen monotherapy was able to push HCV RNA to undetectable levels in four of nine patients. (See *BioWorld Today*, Nov. 8, 2011.)

The paper also broke new ground concerning how microRNAs can affect gene expression.

"To my knowledge, it's the first time that anyone has shown that any microRNA stabilizes any messenger RNA," Lemon said.

A few miRNAs, such as miR-10a, increase the expression of the genes they bind to. But it has not been clear whether they do so by increasing its rate of translation, for example by feeding it into ribosomes more efficiently, or by increasing its stability, which would allow it to be translated more often.

In general, Lemon noted, RNA stability and translation are "really closely connected phenomena," and so which of them is affected by miRNA has been controversial. His team's ability to separate the two fairly cleanly is "one of the nice things about our work." ■

Financings Roundup

• **MacuClear Inc.**, of Plano, Texas, said it secured more than $1 million in funds from current investors for completion of its pivotal, Phase IIIa study of MC-1101, a topically administered eye drop aimed at treating and stopping the progression of dry age-related macular degeneration (AMD) into wet AMD. The company also said it inked a partnership with an undisclosed Pacific Rim pharma partner and investor to finance clinical costs, bridging studies and regulatory development for the drug in that region.

• **Vivo Ventures**, of Palo Alto, Calif., closed its Vivo Venture VII fund at $375 million, bringing the firm's total funds under management to more than $1 billion. Vivo said it plans to invest the capital primarily in later development-stage pharma and medical device companies in the U.S. and in revenue-stage health care companies in greater China. The venture firm also intends to continue its strategy of building companies from scratch, identifying later-stage products with high probability of FDA approvals and investing directly in public companies.

• **XOMA Ltd.**, of Berkeley, Calif., said it signed a $10 million, 42-month secured term loan agreement with GE Capital Healthcare Financial Services to help advance IL-1 beta-targeting candidate gevokizumab (XOMA 052) and for general corporate purposes. In addition, XOMA has issued warrants to purchase 263,158 shares of its common stock exercisable at $1.14 per share. In separate news, the company said it would move its corporate domicile from Bermuda to Delaware and change its name to XOMA Corp.

Washington Roundup

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follow-on biologics may not be a short-term proposition."

Some of the twists and turns on the biosimilar path may work against the makers of innovator biologics. If the brand firms miss the tight statutory deadlines laid out by the BPCIA, they could be hit with substantial patent enforcement penalties, according to the report.

The BPCIA, unlike the Hatch-Waxman Act for traditional generics, does not tightly link FDA approval with patent rights. Thus, "brand-name firms must wholly rely upon the judiciary to stay the release of follow-on biologics into the marketplace," the CRS said.

However, other obstacles may work to the advantage of the innovators, the CRS found. For instance, the lack of a biologic equivalent to the FDA's Orange Book, which lists relevant patents for small-molecule drugs, may place biosimilar applicants at a disadvantage. Without that resource, they can't readily assess the patent positions of the reference biologic. As for those biosimilars that make it to market, they'll have a tough road. The CRS noted that in Europe, where biosimilars have been approved since mid-2003, follow-ons have barely penetrated the market, due to safety concerns, brand loyalty and competitive pricing strategies by innovator companies.

The report illustrated its point with Omnitrope (somatropin [rDNA origin], Sandoz GmbH), which has claimed only 1 percent of the $831 million European human growth hormone market. Its slow uptake is attributed to doctors' unwillingness to change products, issues with delivery mechanisms and prices that are "only" 20 percent to 25 percent below that of the innovator. (See *BioWorld Today*, July 26, 2011.)

Since the biosimilar pathway is still under construction, CRS predicted some considerable changes could be in the works – and not just for biosimilars. Reading between the lines of the BPCIA, the CRS said the patent dispute resolution system included in the act suggested congressional dissatisfaction with the Hatch-Waxman Act, which sparked a seemingly endless round of patent suits and settlements. It also suggested a desire to try new approaches. (See *BioWorld Today*, June 29, 2011.)

The CRS' conclusion? "Individuals interested in pharmaceutical patent law would be wise to remain vigilant concerning developments to the new law of follow-on biologics in coming years," it said.

Bill Would Speed Access to Orphan Drugs

One of the final pieces of legislation introduced in Congress last year would speed approval of treatments for ultra-rare diseases. In introducing the Unlocking Lifesaving Treatments for Rare-Diseases Act, or ULTRA, Rep. Cliff Stearns (R-Fla.) said that the FDA's approval rate for drugs has slowed immensely. His bill, H.R. 3737, is intended to remedy that by allowing surrogate endpoints to be used in the accelerated approval of fast-track drugs aimed at ultra-rare diseases.

The bill also calls for guidance, within one year, on qualifying surrogate endpoints without supporting clinical data. It stipulates that in qualifying a surrogate endpoint, the FDA must balance other considerations, such as:

- the unmet need the drug is intended to address, and the adverse effects the disease is likely to have on the quality or length of life;
- the very low likelihood that supportive data would exist or that studies could be completed to support the surrogate, given the small size of the patient population and other barriers;
- the full scope of available scientific information.

Stearns noted that at a hearing he held last year, he "found that the FDA has not used all the tools available to them to help bring new drugs to market to treat rare and ultra-rare diseases."

H.R. 3737 has been referred to the House Energy & Commerce Committee.

OIG Seeks Anti-Kickback Safe Harbor Ideas

While the Department of Justice is cracking down on drug companies that violate the federal anti-kickback law, the Department of Health and Human Services Office of Inspector General (OIG) is taking suggestions on safe harbors from that law. "Since the statute on its face is so broad, concern has been expressed for many years that some relatively innocuous commercial arrangements may be subject to criminal prosecution or administrative sanction," the OIG said in a *Federal Register* notice Tuesday.

In response to that concern, OIG is annually tasked with ensuring that safe harbor provisions appropriately limit the reach of the statute. Recommendations for developing new or modified safe harbor regulations should be submitted to the public docket OIG-120-N by Feb. 27. ■

Other News To Note

- **Amgen Inc.**, of Thousand Oaks, Calif., said the FDA has invited the company to participate in a meeting of its Oncologic Drugs Advisory Committee (ODAC) on Feb. 8 to discuss the supplemental biologics license application (sBLA) for Xgeva (denosumab) in men with castration-resistant prostate cancer (CRPC) at high risk of developing bone metastases. The ODAC will review results from clinical studies in support of the new indication, including the pivotal '147 trial, a randomized, placebo-controlled, multicenter Phase III study that compared Xgeva to placebo in prolonging bone metastasis-free survival in men with non-metastatic CRPC at high risk for bone metastases based on prostate-specific antigen criteria. Amgen submitted the sBLA for Xgeva's second indication on June 27, 2011, and the application has a PDUFA date of Apr. 26, 2012. (See *BioWorld Today*, Nov. 22, 2010, and Sept. 16, 2011.)

Clinic Roundup

• **Affitech A/S**, of Copenhagen, Denmark, said its Russian partner, **IBC Generium**, submitted a clinical trial application to the Russian Health Authority to begin a Phase II trial with Affitech's lead monoclonal antibody candidate AT001/r84. The anti-VEGF antibody will be evaluated in patients with various cancers and is a possible competitor to bevacizumab (Avastin, Roche AG).

• **Agile Therapeutics Inc.**, of Princeton, N.J., completed the final Phase III trial of AG200-15 and is on track to submit the new drug application (NDA) for the combination hormonal contraceptive patch to the FDA during the first quarter. The patch, in two Phase III trials enrolling more than 2,000 women, demonstrated its ability to deliver a low dose of ethinyl estradiol and a dose of levonorgestrel consistent with the efficacy and safety profiles of low-dose oral contraceptives. The patch is intended to be applied once weekly for three weeks, followed by a fourth, patch-free week.

• **Ampio Pharmaceuticals Inc.**, of Greenwood Village, Colo., completed the expanded enrollment phase of its Ampion in knee trials in Australia, adding 42 patients to the original placebo-controlled, 60-subject study. No adverse events were reported in the initial study of Ampion, a naturally occurring human molecule being developed to treat chronic pain. Results from the original trial are expected to be available in the next four to six weeks.

• **BioMarin Pharmaceutical Inc.**, of Novato, Calif., plans to initiate a Phase I safety and dosing trial for BMN-111 in healthy adults in the first quarter. An analogue of C-type natriuretic peptide, BMN-111 is being developed to treat achondroplasia, the most common form of dwarfism. BioMarin expects to start a Phase II study in pediatric subjects late this year or early 2013.

• **Can-Fite BioPharma Ltd.**, of Petah-Tikva, Israel, said its 18-patient Phase I/II study of CF102 met its objectives, with the drug showing a favorable safety profile in patients with hepatocellular carchoma and Child-Pugh cirrhosis classes A and B. The median overall survival time was 7.8 months. The median overall survival time of the Child-Pugh B patients was 9.4 months, which the company said is the longest overall survival time reported in literature for that patient population. A separate Phase I/II study in patients with hepatitis C also reached its objectives of safety and pharmacokinetic behavior. CF102 is an oral drug designed to bind to the A3 adenosine receptor.

• **Osiris Therapeutics Inc.**, of Columbia, Md., said an interim assessment at one year of its Phase II trial evaluating Prochymal in patients with newly diagnosed Type I diabetes showed systemic infusions of the adult mesenchymal stem cells (MSC) were well-tolerated, but no significant differences in the rates of disease progression, measured by stimulated C-peptide levels, have been observed. There was a trend toward fewer hypoglycemic events for patients treated with Prochymal as compared with controls. The patients will be followed for another year. The trial, conducted in partnership with JDRF, is testing MSCs from unrelated adult donors in 63 pediatric and adult patients.

• **Yakult Honsha Co. Ltd.**, of Tokyo, initiated a Phase I/II trial in Japan to assess the safety and efficacy of perifosine in combination with capecitabine in patients with refractory advanced colorectal cancer. Under a potential $69 million partnership agreement signed last year, the start of the trial triggers a milestone payment of an undisclosed amount to **Aeterna Zentaris Inc.**, of Quebec City. Meanwhile, a U.S. Phase III trial of the PI3K/Akt inhibitor in colorectal cancer is expected to be completed in the first quarter. (See *BioWorld Today*, March 10, 2011.)

Other News To Note

• **Apogenix GmbH**, of Heidelberg, Germany, said it received an additional €2.3 million BMBF (German Federal Ministry of Education and Research) grant for the further advancement of lead candidate APG101, a fully human protein designed to inhibit the CD95 ligand. Apogenix will use the proceeds to develop APG101 in myelodysplastic syndromes, specifically for the production of clinical material and the development of a biomarker program.

• **Apricus Biosciences Inc.**, of San Diego, and **Stellar Pharmaceuticals Inc.**, of Milton, Ontario, signed an exclusive license agreement for the commercialization of Apricus Bio's MycoVa product for onychomycosis (nail fungus) in Canada, following receipt of Canadian regulatory approval. The agreement provides for up to C$8 million (US$7.918 million) in an up-front payment, regulatory approval milestone and sales achievement milestones to Apricus Bio, plus tiered double-digit royalty payments during the multiyear agreement. MycoVa combines the approved nail fungus drug terbinafine with Apricus Bio's NexAct technology to enhance drug absorption through the skin.

• **Astex Pharmaceuticals Inc.**, of Dublin, Calif., said the FDA's Oncologic Drugs Advisory Committee will discuss its supplemental new drug application for Dacogen (decitabine) for Injection at its Feb. 9, 2012, meeting. The proposed indication for the application is elderly acute myelogenous leukemia. (See *BioWorld Today*, April 8, 2011.)

• **Axerion Therapeutics Inc.**, of New Haven, Conn., said data published by Yale University in *Annals of Neurology* demonstrated that Nogo decoy receptor (NgR) is effective in a preclinical model of chronic spinal cord injury. Treatment for three months allowed 29 percent of injured animals to regain the ability to bear weight and walk, compared to no recovery found in animals treated with an inactive control protein.

• **BioTime Inc.**, of Alameda, Calif., said it elected to market progenitors of muscle stem cells bearing hereditary diseases and will produce products from five human embryonic stem cells lines from the Reproductive Genetics Institute of Chicago. The muscle cell lines will display the genes for Duchenne's muscular dystrophy, Emery-Dreifuss muscular dystrophy, spinal muscular dystrophy Type 1, facioscapulohumeral muscular dystrophy 1A and Becker muscular dystrophy.

• **Cell Therapeutics Inc.**, of Seattle, said the FDA's Oncologic Drugs Advisory Committee will review on Feb. 9 the firm's resubmitted new drug application for pixantrone in relapsed or refractory aggressive non-Hodgkin's lymphoma patients who have failed two or more lines of prior therapy. The aza-anthracenedione candidate received a complete response in 2010, and the firm's appeal to the FDA last year was unsuccessful. (See *BioWorld Today*, April 12, 2010, and May 4, 2011.)

• **Chelsea Therapeutics International Ltd.**, of Charlotte, N.C., said the FDA scheduled a meeting of the Cardiovascular and Renal Drugs Advisory Committee on Feb. 23 to review its new drug application (NDA) for Northera (droxidopa), an orally active synthetic precursor of norepinephrine, for symptomatic neurogenic orthostatic hypotension in patients with primary autonomic failure, dopamine beta hydroxylase deficiency and nondiabetic autonomic neuropathy. Chelsea submitted the NDA and requested priority review on Sept. 28, 2011. The application has a PDUFA date of March 28, 2012. (See *BioWorld Today*, Sept. 29, 2011.)

• **CSL Behring**, of King of Prussia, Pa., said the FDA approved a label expansion for self-administration of Berinert, (C1 esterase inhibitor [human]) for treating acute attacks of hereditary angioedema (HAE). As part of the label expansion, Berinert also now is indicated to treat life-threatening laryngeal HAE attacks, as well as facial and abdominal attacks.

• **Generex Biotechnology Corp.**, of Worcester, Mass., said it is accelerating development of cancer vaccine AE37 following positive interim Phase IIb data reported last month at the San Antonio Breast Cancer Symposium. The company said it plans to organize an end-of-Phase II meeting with the FDA by the end of the first quarter to move the Ii-Key hybrid-based HER2/neu peptide vaccine into a pivotal program in women with loco-regional breast cancer that express low to moderate levels of HER2. Parallel steps will be taken with the European Medicines Agency.

• **MultiCell Technologies Inc.**, of Woonsocket, R.I., said it received the final cash grant award payment of $303,102 under the Qualifying Therapeutic Discovery Project program.

• **NovaBiotics Ltd.**, of Aberdeen, UK, said it received orphan designation in Europe for Lynovex (cysteamine), its dual mucolytic-antibacterial drug in development for cystic fibrosis. That designation would provide 10 years of marketing exclusivity in the European Union upon approval. The company is in discussions with prospective partners to license or co-develop the drug.

• **Phylogica Ltd.**, of Perth, Australia, inked a collaboration and option agreement with Janssen Biotech Inc., a unit of New Brunswick, N.J.-based **Johnson & Johnson**, to discover new classes of drugs derived from Phylogica's Phylomer peptide platform. In the initial stage of the collaboration, Phylogica will identify cell-penetrating Phylomer peptides. Under the terms, Janssen could develop Phylomer-based drug candidates and has the option to expand the scope of the deal to include additional cell-specific Phylomers for the development of a further 10 candidates. Phylogica gets an initial fee, as well as research funding over the first 18 months, and could receive further research funding, license fees, milestone payments and royalties on worldwide product sales.

Other News To Note

• **Poniard Pharmaceuticals Inc.**, of Seattle, said Nasdaq determined to delist the firm's common stock and suspended trading as of Jan. 3. The company's stock is expected now to be listed on the OTCQB under "PARD." Last month, Poniard said its proposed merger with Seattle-based **Allozyne Inc.** had fallen through. The companies inked the deal in June to combine Allozyne's pipeline with Poniard's public listing, but the firms later determined that the common stock of the combined company would not qualify for a listing on Nasdaq. (See *BioWorld Today*, June 24, 2011.)

• **Regeneron Pharmaceuticals Inc.**, of Tarrytown, N.Y., said it signed a nonexclusive license and partial settlement agreement with South San Francisco-based **Genentech Inc.** (now part of the Roche Group) relating to U.S. ophthalmic sales of Eylea (aflibercept). Under the terms, Regeneron will make payments to Genentech based on sales of the wet age-related macular degeneration drug through May 7, 2016. The firm will pay $60 million upon cumulative U.S. sales of Eylea reaching $400 million, plus royalties of 4.75 percent on cumulative U.S. sales between $400 million and $3 billion and 5.5 percent on any cumulative sales topping $3 billion. Regeneron received a nonexclusive license to certain patents relating to VEGF receptor programs. Known as the Davis-Smyth patents, they are the subject of patent litigation between Regeneron and Genentech, now pending in District Court. Eylea was approved in November. (See *BioWorld Today*, Nov. 22, 2011.)

• **Senesco Technologies Inc.**, of Bridgewater, N.J., said the combination of Revlimid (lenalidomide, Celgene Corp.) and SNS01-T performed better than either treatment alone in mouse xenograft models of human mantle cell lymphoma. When SCID mice, implanted with an aggressive human mantle cell lymphoma cell line (JVM2), were treated with either 15 mg/kg lenalidomide (five times weekly by intra-peritoneal injection) or 0.375 mg/kg SNS01-T (twice weekly by intravenous injection) there was a growth delay of four days and 14 days, respectively. Mice treated with a combination of both drugs using the same dose levels and dosing regimens exhibited a tumor growth delay of 27 days ($p = 0.0008$).

• **TrovaGene Inc.**, of San Diego, said it obtained an exclusive worldwide license to mutations of the SF3B1 splicing factor, which have been shown to be associated with disease progression and chemotherapy response in patients suffering from chronic lymphocytic leukemia. Research published in *Blood* suggested that SF3B1 mutations represent important incremental diagnostic markers beyond TP53 disruptions and NOTCH1 mutations in CLL patients and may provide a therapeutic target for SF3B1 inhibitors, which currently are in preclinical development. Terms of the license agreement were not disclosed.

• **Zealand Pharma A/S**, of Copenhagen, Denmark, received €3 million (US$3.917 million) in milestone payments under a potential €140 million license agreement with **Helsinn Healthcare SA**, of Lugano, Switzerland, for the development of elsiglutide (ZP1846), a GLP-2 peptide agonist, for chemotherapy-induced diarrhea. Helsinn is completing a Phase Ib study of elsiglutide in Europe to evaluate safety and tolerability and determine the maximum tolerated dose in colorectal cancer. The study, conducted under an FDA investigational new drug application, is expected to conclude this quarter. In parallel, Helsinn is preparing a Phase IIa study to evaluate the efficacy of elsiglutide in the primary prevention of diarrhea in colorectal cancer patients receiving chemotherapy. (See *BioWorld Today*, Dec. 2, 2008.)

U.S. Patent Disclosures

• **Vermillion Inc.**, of Austin, Texas, received a notice of allowance for a patent, titled "Beta-2 Microglobulin (B2m) and C Reactive Protein (CRP) as Biomarkers for Peripheral Artery Disease." It covers the use of that combination of biomarkers for the diagnosis of peripheral artery disease.

• **Virxsys Corp.**, of Gaithersburg, Md., received U.S. Patent No. 8.041,633, which broadens the firm's lentiviral vector stable cell line platform for large-scale production capabilities. It also was awarded U.S. Patent No. 8,053,232, which covers the company's ability to treat human diseases with its SMaRT technology platform, and in particular, patients with alpha-1-antitrypsin deficiency.