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BIO 2011 International Convention

Innovation as Critical as Funding for Long-Term Health of Biotech

By Jennifer Boggs
Assistant Managing Editor

WASHINGTON – As the financing track kicked off with its first BIO2011 session in a crowded room at the Walter E. Washington conference center, the focus was on how to access National Institutes of Health (NIH) grants and other funding sources to get early stage research across the so-called Valley of Death.

But panelists in a later business development session discussed what could prove even more damaging to the biotech industry in the long term: the innovation gap.

It's no secret that R&D productivity has declined over the past decade, so much so that big pharma – some made even bigger thanks to recent mega-mergers – is increasingly turning to biotech to fill its dwindling pipelines.

See Innovation, Page 8

Biosimilar IP Strategies Call for Intricate Choreography

By Mari Serebrov
Washington Editor

WASHINGTON – Compared with the abbreviated new drug process, the biosimilar pathway looks like an intricately choreographed dance of notification, disclosure and negotiations between the innovator and the follow-on.

The complex footwork may have some biosimilars thinking it's not worth the effort, especially since one of the steps requires them to disclose their confidential information.

The pathway sets a rigid dance schedule for innovators and follow-ons to discuss patents that may be infringed. It starts with a 20-day period in which the biosimilar applicant must provide the innovator with a copy of its

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Day 1 of Avastin Hearing Brings Emotional Anecdotes, Hard Facts

By Marie Powers
BioWorld Today Contributing Writer

A parade of three dozen physicians, nurses, patients, advocates and family members overwhelmingly endorsed the continued availability of Avastin (bevacizumab) for metastatic breast cancer during the first day of the FDA's unprecedented hearing on its proposal to withdraw the drug's approval for the indication. But in a slew of legal and scientific data, representatives from the FDA's Office of New Drugs and Center for Drug Evaluation and Research laid the groundwork for an unflinching rejection of the request by Genentech Inc., of South San Francisco, and parent company Roche AG, of Basel, Switzerland, to continue marketing the

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Financings Roundup

Investors Pony Up \$27M for Acetylon's HDAC6 Inhibitors

By Trista Morrison
Staff Writer

With early stage venture funding hard to come by, Acetylon Pharmaceuticals Inc. has found an alternative way to fund its development of isoform-selective histone deacetylase (HDAC) inhibitors. The Boston-based biopharma has raised \$27 million in Series B financing from a large contingent of private individuals.

Acetylon used a similar strategy with its \$7.25 million Series A round in 2009. President and CEO Walter Ogier said the company didn't set out to avoid the traditional venture route, but the round "quickly became oversubscribed."

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BIO 2011

New Rare Disease Group to Increase Number of Drugs

By Nuala Moran

BioWorld Today Correspondent

WASHINGTON – An international consortium is about to launch with an ambitious target to develop diagnostics for the majority of the 8,000 known rare diseases and to increase the number of registered drug treatments available for these conditions from 200 currently to 400 by 2020.

The International Rare Diseases Research Consortium (IRDiRC) has been formed by the European Commission and the U.S. National Institutes of Health, with countries including Canada, Japan, the UK and Italy having expressed an interest in taking part. To date the consortium has held two meetings to begin to scope its objectives and draw up a strategy, and a third meeting will be held in Montreal in October where it is intended to finalize the program.

“We think the time is right to look at rare disease from a system approach, capitalizing on genomics to speed up processes and address several diseases at the same time, Indridi Benediktsson of the European Commission told delegates at BIO 2011.

Andrzej Rys, director of public health at the European Commission’s Health Directorate said IRDiRC will network the best scientists in the world to work on understanding the pathophysiology of rare disease, carry out genomic analyses, develop in vitro and in vivo models, ontologies and plot the natural history of those conditions. In addition, there will be grant programs to develop biomarkers, support for building and sharing of patient registries and support for clinical trials.

“The European Commission wants to push the agenda and increase our commitment in the coming years,” Rys said.

Rare diseases are a global health issue noted Stephen Groft, director of the NIH Office of Rare Diseases. “As the consortium gathers more partners, the needs are the same regardless of country.” Increasing the number of new therapies by 200 by 2020 will involve doubling the

Stock Movers

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Company	Stock Change	
Nasdaq Biotechnology	+\$20.74	+1.92%
Adolor Corp.	+\$0.19	+10.05%
Endocyte Inc.	+\$0.97	+7.36%
Genmab	+\$4.13	+11.45%
Palatin Technologies Inc.	+\$0.14	+16.67%
YM Biosciences Inc.	+\$0.19	+7.09%

(Biotechs showing significant stock changes Tuesday)

current rate of approvals. To do this, “There will be a major emphasis on repurposing products that are on the market or in human [trials],” Groft said. The objective of developing new diagnostics for 8,000 rare diseases is a “tremendous task,” but, said Groft, “Genome sequencing means we can do diagnostics more easily.”

Beyond learning more about rare diseases, a lot of work is needed to share information widely. The IRDiRC needs to establish and link up a global rare diseases community, Groft said.

The Montreal meeting will aim to identify the best mechanism to meet these goals and establish a governance structure. The meeting will also consider the perspectives and needs of industry. In addition, regulators will be invited to discuss their needs and concerns, around trial size and trial design. “There are many ethical considerations to rare diseases research,” Groft noted. For example, what is the role of placebo, are there opportunities for adaptive trial design.

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Lynn Yoffee, **(404) 262-5408**
Jennifer Boggs, **(404) 262-5427**
Anette Breindl, **(518) 595-4041**
Trista Morrison, **(858) 901-4785**
Mari Serebrov, **(703) 678-7376**
Tom Wall, **(404) 262-5417**

Senior Vice President/Group Publisher:
Donald R. Johnston, **(404) 262-5439**
Internet: <http://www.bioworld.com>



Rare Diseases

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The hope is that regulators can be persuaded to merge their authorization procedures. "There is certainly a need for this," Groft said.

New Appeal for Biotechs

Big pharma's newly emerging interest in rare diseases has also heightened their appeal for biotechs, given the increased opportunities for partnering that pharma's fascination provides, as discussed during a session at BIO2011 on rare diseases.

But while the pace and scale of deal-making around orphan drugs has grown substantially, there remain significant problems in areas such as patient identification, convincing regulators to grant approvals on the basis of small trials, and in pricing and reimbursement.

Like many rare genetic diseases, the bone disorder hypophosphatasia presents in a range from severe cases in childhood to adult onset. "It's a very heterogeneous picture and therefore a real challenge to developing the therapy," said Julie Smith, chief commercial officer of Enobia Pharma Inc., which is developing an enzyme replacement therapy. "The full spectrum of the disease is not appreciated, but you have to select patients for trials."

The disease is classified as having subtypes, but in fact these are a continuum. There is low awareness of the disease, a lack of understanding of its natural history and a lack of information on market size. It is difficult to tease these three aspects apart to quantify the size of the value of the market, and this is a picture that is replicated in many ultra-orphan diseases, Smith noted.

Three elements must be triangulated together to calculate overall market size: epidemiology; sparse market data and physician and patient information. Many obstacles stand in the way of extracting reliable data, including the fact that often there is no classification for a rare disease, meaning it is not possible to search medical records. Forecasting market size on the basis of mutation screening to pick out the disease genotype almost always leads to overestimates, while looking for the phenotype leads to underestimates because it relies on accurate diagnosis.

In a few countries there are reliable patient registries, but it remains difficult to get meaningful data on most rare diseases. One source of growing importance is social media sites. "Patients are communicating internationally," Smith said. However, she cautioned people to be transparent about why they have signed up to online sites and the use to which they intend to put intelligence gathered in this way.

Following a survey of 69,996 physicians across the U.S., France, the UK, Germany, Canada, Japan and Brazil, Enobia identified 2,040 patients. "In other words, you need a big market research budget to find a few patients," Smith said.

Finally, she cautioned, "Don't count a patient in a market forecast until you've seen the whites of their eyes."

Jeff Behrens, senior director, business development and operations at Edimer Pharmaceuticals Inc., agreed that building relationships with patients is of critical importance in developing treatments for ultra rare diseases. In the case of Edimer, which is developing a treatment for X-linked hypohidrotic ectodermal dysplasia, the drug needs to be administered within the first week of life.

There is a gene test for carriers, and so Edimer's strategy is revolving around enrolling women while they are pregnant.

Although there is more interest in rare diseases among pharma, finding the right partner remains a fraught process, suggested Cyrus Mozayeni, senior director of business development at Bluebird Bio Inc.

The company has clinical proof of concept for its gene therapy platform in treating two ultra orphan diseases. It now wants to leverage this to rare diseases. "For us, it's about gene therapy, not just rare diseases. We need to be an integral partner for it to be successful. We have a lot of expertise and know these programs better than anyone else," Mozayeni said. ■

Other News To Note

- **Amgen Inc.**, of Thousand Oaks, Calif., filed a supplemental new drug application with the FDA to expand approval for Xgeva (denosumab) to reduce the risk of bone metastases in men with castrate-resistant prostate cancer. The submission is based on Phase III data showing that Xgeva significantly prolonged bone metastasis-free survival by more than four months compared with placebo. Xgeva is already approved for the prevention of skeletal-related events in patients with bone metastases from solid tumors. (See *BioWorld Today*, Dec. 15, 2010.)

- **Chimerix Inc.**, of Durham, N.C., said the Department of Health and Human Services' Biomedical Advanced Research and Development Authority (BARDA) amended its sole source contract with **SIGA Technologies Inc.** for 17 million courses of smallpox antiviral as well as an optional 12 million additional courses. BARDA removed the 12 million course option from the contract, which would allow Chimerix or other competitors to bid against SIGA on future contracts for the remaining amount. Chimerix dropped its Government Accountability Office protest, and SIGA can now move forward delivering smallpox drug ST-246. (See *BioWorld Today*, May 17, 2011.)

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BIO 2011

Financing Platform Companies: Funds are There if You Deliver

By Tom Wall
Staff Writer

WASHINGTON – Getting funding for candidates beyond the lead compound continues to be a challenge for platform companies with multiple programs. Where's the money coming from today – venture capital, partners, government grants, sovereign funding or foundation support?

If you can deliver results, all of the above, said leaders of four platform companies during a financing breakout – “Beyond the Lead Compound: Attracting Funding for Multiproduct Platforms” – at the BIO 2011.

“To do it justice, you have to do all of the above,” said panelist Scott Minick. “You have to think more broadly than just the traditional ways of funding.”

Panelists included Minick, president and CEO of the Cambridge, Mass.-based nanoparticle specialist BIND Biosciences Inc., whose company has raised a total of \$42 million since 2007; Dominick Colangelo, president and CEO of Promedior, of Malvern, Pa., a company whose immune-targeted approach to treating fibrotic disease has raised \$41 million since its founding in 2006; Guy Macdonald, president and CEO of the Watertown, Mass.-based antibiotic developer Tetrphase Pharmaceuticals Inc., which has raised \$80 million since its founding in 2006, including a \$45 million Series C last June; and John Mendlein, executive chairman of aTyr Pharma Inc. and Fate Therapeutics Inc., both of San Diego.

Fate, which is developing small-molecule drugs aimed at modulating adult stem cells, has attracted a total of \$50 million, while aTyr has stimulated investor interest with its research on physiocrines, has raised a total of \$47 million. The panel was moderated by Polaris Venture Partners' General Partner Alan Crane.

“This is really a difficult time for everybody involved,” Colangelo said. “It does cause us to be more focused than we want to be. But you can raise capital based on the results you produce. If you show results, you will be able to attract capital, but that doesn't mean you can go off and do everything you want to do.”

Macdonald said that it is important to have investors who are aligned on the platform company's strategy. “When you get to Phase I and Phase II the price goes up dramatically and you can find out that investors are not aligned. Even when you think everybody is aligned, things can change.”

Minick said that he is convinced that “the right way to start a platform biotech company is with venture capital.” But, he noted, some firms understand platform companies and others don't. “You want investors who really know what platform means,” he said, adding that when push comes to shove, investors who don't will want to pick a winner from multiple candidates and forego platform development.

But Minick said it is important to involve more than venture investors as a platform advances. “You have to evolve the funding of platforms, just as the platform itself evolves,” he said.

Mendlein agreed that it is important to go beyond venture funds and try to find strategic investors, who he defined as people who don't want to miss the next great direction in therapeutic development. “I think there are some real opportunities to leverage venture, but also to look at big biotechs or big pharmas who are using their venture arms as well.”

Mendlein and Minick both cautioned that partnerships, while providing funding, can also compromise the platform company's original goals.

“The key is to not give up too much of the strategic footprint,” Mendlein said. “If you give up too much, what do you have left for yourselves that you want to develop? We want to be able to create a pipeline for our investors that also is accessible for our partners.”

“You can overdo a good thing,” Minick added. “If you work with everybody, what's your exit? You might reduce the exit value of the company if you go too far down the road of partnering.”

Colangelo and Macdonald both said that government grants are a good source of nondilutive dollars.

Colangelo noted that Promedior has received funding from the National Institutes of Health to advance research on reducing fibrosis after radiation. “That's an instance where stockpiling initiatives can benefit a company,” he said. “It can lead to some interesting government funding.”

Macdonald said the challenge is “to get grants in a program we really want to do. You have to be very careful that the grant adds value in a program we otherwise couldn't bring forward, or that it supports the lead compound.” ■

Other News To Note

• **Critical Outcome Technologies Inc.**, of London, Ontario, said lead oncology product COTI-2 demonstrated significant single-agent efficacy in an animal model of human ovarian cancer overexpressing Akt. Partial and complete tumor regressions were observed at two dose levels, with significantly more complete remissions in the high-dose group compared to control. COTI-2 is a small-molecule inhibitor of Akt/PKB phosphorylation.

• **Gilead Sciences Inc.**, of Foster City, Calif., entered a license agreement with New Brunswick, N.J.-based **Johnson & Johnson** subsidiary Tibotec Pharmaceuticals to develop and commercialize a fixed-dose combination of Gilead's Phase III boosting agent cobicistat and Tibotec's FDA-approved protease inhibitor Prezista (darunavir) for HIV. Tibotec will be responsible for the formulation, manufacturing, registration, distribution and commercialization of the combination product worldwide. Terms were not disclosed.

BIO 2011

Pay Now or Pay Later? Don't Ignore Importance of Phase II

By Jennifer Boggs

Assistant Managing Editor

WASHINGTON – For drug development firms trying to save money or playing catch-up in a highly competitive field, it might seem a good idea to skimp on Phase II testing by enrolling fewer patients, conducting only one midstage study or even leapfrogging straight to Phase III and hoping that the efficacy signal observed in Phase I wasn't just a fluke.

But companies failing to spend the time in Phase II do so at their peril, according to speakers during a Tuesday morning session focused on de-risking the Phase II to Phase III advancement decision.

In fact, Lisa Natanson, senior analyst at Deloitte Recap LLC, said the odds of reaching market greatly increase for products that have undergone two or more Phase II studies before advancing into pivotal trials. A report by Deloitte that looked at 33 biotech compounds that were late-stage terminations – either at Phase III or at filing – and at 64 compounds that have gained approval in the past decade showed that 70 percent of failed compounds were tested only in one study. Nine percent of failed compounds skipped Phase II altogether.

The majority (58 percent) of approved compounds, however, went through more than one Phase II trial before starting pivotal programs.

Companies with the successful products also invested more in Phase II, running larger studies. The average Phase II enrollment for failed compounds was 69 patients, while successful compounds were tested in an average of 171 patients per Phase II trial, Natanson said.

Interestingly, she noted, companies with failed compounds invested more in Phase III development. Enrollment in Phase III averaged 821 patients per Phase III trial vs. 697 patients per trial for the approved drugs.

The majority (61 percent) of drugs advanced based on a single Phase II study had what Natanson called “high-risk evidence,” meaning a neutral or even negative efficacy signal in the Phase II study. So it's no surprise that more than half of them disappointed in Phase III.

Of the drugs that made it through to approval despite only one Phase II trial, only 19 percent involved high-risk evidence.

“It's not that you can't” be successful based on one Phase II trial, Natanson said, but there's no question that companies will have to put in the time – and money – one way or another.

Human Genome Sciences Inc., for example, only ran one Phase II study for now-approved lupus drug Benlysta (belimumab). That much-maligned trial missed its endpoints, which measured a reduction in signs and

symptoms at week 24, using the Safety of Estrogens in Lupus Erythematosus National Assessment Systemic Lupus Erythematosus Disease Activity Index (SELENA SLEDAI) and measured the time to first lupus flare over a 52-week period using the British Isles Lupus Assessment Group (BILAG) scale. (See *BioWorld Today*, Oct. 6, 2005.)

The Rockville, Md.-based firm was convinced that the science was solid. Benlysta targets the BLYS protein and had shown in early research to work by inhibiting the high BLYS levels that prompt autoantibodies to attack healthy tissues in lupus patients. But there were “major gaps in our knowledge” of quantitative assessments for the disease, said David Stump, executive vice president of R&D for HGS.

Company execs realized they would need to better understand those assessments. “We knew we were signing up for a major analytical process” at the end of the Phase II trial, he said.

HGS reviewed everything from patient identification – those who tested positive for autoantibodies were more likely to respond to the drug – to the specific measuring scales.

At the end of analysis, the company reached agreement with the FDA on a composite endpoint for two planned Phase III trials. (See *BioWorld Today*, Aug. 10, 2006.)

The endpoint had three components: at least a four-point reduction from baseline in SELENA SLEDAI score, no worsening in Physician's Global Assessment and it measured organ damage using the BILAG scale.

Coming up with that endpoint was “critical to moving forward,” Stump said.

And the Phase II analysis paid off. Benlysta hit its endpoints in both Phase III trials and went on to become the first new drug approved for lupus in 56 years. (See *BioWorld Today*, March 11, 2011.)

So it is possible to only do one Phase II trial, “but you have to learn from it,” Stump said.

Yet, as in life, drug development comes with no guarantees.

“We made a rational decision, but we had some luck, too,” Stump acknowledged. “You have to stack the deck and play the hand. It's an odds game.” ■

Other News To Note

• **Novelos Therapeutics Inc.**, of Madison, Wisc., said a District Court dismissed the putative federal securities fraud class action lawsuit against the company. The suit was related to statements made regarding lung cancer drug NOV-002 before it failed a Phase III trial. (See *BioWorld Today*, Feb. 25, 2010.)

• **Pfizer Inc.**, of New York, said the FDA accepted for review its new drug application for axitinib in renal cell carcinoma. The selective inhibitor of VEGF receptors 1, 2 and 3 is also under review in Europe.

BIO 2011

Partnering or Acquisition? Two Companies Share Their Stories

By Catherine Shaffer

BioWorld Today Contributing Writer

WASHINGTON – Most biotech start-ups, even the most successful, will at some point hit a cash flow wall, where they need a large infusion of funding to get a product to the regulatory finish line. Recent economic trends have largely taken the initial public offering (IPO) option off the table, so for most companies the choice comes down to partnering or acquisition. At BIO 2011, Calistoga Pharmaceuticals Inc. CEO Carol Gallagher and Athersys Inc. CEO Gil Van Bokkelen discussed how they arrived at the decision to partner or sell.

Additional experts joining the conversation were Hoffman La-Roche Global Director of Strategic Partnering Robert Silverman, New Enterprise Associates Principal Ali Behahani, and Pappas Ventures' Scott Weiner.

Seattle-based Calistoga closed one of the largest biotech M&A deals of 2011 with Gilead Sciences Inc. in February for \$375 million in up-front cash and \$225 million in potential milestones. Calistoga's lead compound CAL-101 (now GS 1101), a compound targeting phosphoinositide-3 kinase (PI3K), was in Phase II trials as a single agent on non-Hodgkin lymphoma and in combination with rituximab in chronic lymphocytic leukemia. The acquisition helped to round out Gilead's early midstage oncology and inflammatory disease pipeline. The company had acquired two other companies previously in the areas of cancer and rheumatology.

Gallagher said the successful exit event for Calistoga began as a partnering quest. "The challenge for us in the early days was to think strategically about the capital we needed. . . . We felt confident we could develop the drug ourselves," she said.

CA-101 was the only drug with that specific mechanism in clinical trials at the time. It gave the company a three-to-four year lead on its competition. The challenge was running parallel development. The company wanted to pursue registration trials in more than one indication, a capital-intensive proposition. It began looking for North American partnerships, and talking to investors and to pharma.

As it turned out, a number of companies were interested in the lucrative North American licensing rights to CA-101. Gallagher responded that those rights were a large part of Calistoga's value, and that they couldn't sell them.

A number of companies countered with acquisition offers, leading to the Gilead's \$600 million purchase.

"Companies are bought not sold," said Gallagher, who advises biotech leaders to use the principle of Best Alternative to a Negotiated Agreement (BATNA). Because Calistoga had a BATNA, and had already done the work of creating a valuation on the company before entering partnering negotiations, it was able to easily shift gears to M&A negotiations, and make a good deal for its stakeholders.

Athersys took the other fork in the road, shaking hands with Pfizer Inc. in 2009 for a \$111 million licensing deal for development of its adult stem cell platform for inflammatory bowel disease. (See *BioWorld Today*, Dec. 22, 2009.)

Like Calistoga, Cleveland's Athersys needed to pursue multiple indications for its Phase I product, MultiStem. It already had a partnering relationship with Angiotech Pharmaceuticals Inc. for cardiovascular disease.

Bokkelen said that the company was aware from an early stage that it could not predict what disease indications would be most successful for MultiStem. It attacked the problem by developing relationships with dozens of investigators at 30 institutions in the U.S. and Europe.

That helped it determine where the product has relevance, without "going deep" in one disease area.

Once it had built that foundation of data, it was able to take a segmented approach to partnering. Bokkelen stressed the importance of looking at the big picture.

Each deal has been structured to provide Athersys and its stakeholders a meaningful share of the downstream proceeds. Under the terms of its 2009 deal with Pfizer, Athersys received \$6 million up front, plus \$105 million in potential milestones in the area of inflammatory bowel disease. It also received research funding and support through the initial phase of the collaboration.

Pfizer took responsibility for regulatory and commercial development, paying Athersys tiered royalties on worldwide sales of MultiStem IBD products. "We spent a lot of time focused on what is a working relationship," Bokkelen said. "It was not just a handoff – throw it over the fence and say let us know when our next milestone payment is due. That's not the best way to protect value for stakeholder."

Even a carefully planned segmented partnering strategy like Athersys's can turn into an acquisition, given the right circumstances. Robert Silverman gave two examples of companies that had partnered programs that were acquired by other companies.

When Roche acquired Marcadia Biotech Inc. in January, it already had a program partnered with Merck dating to 2008. That did not turn out to be an impediment to Roche's acquisition. "That turned into an M&A despite the fact that the company had a more advanced program it had already partnered," he said. (See *BioWorld Today*, Jan. 3, 2011.)

Daiichi Sankyo Co. Ltd. had no doubts about snatching up longtime Roche development partner Plexxikon Inc. in March for \$805 million up front and \$130 million in milestones for PLX4032. (See *BioWorld Today*, March 2, 2011.)

Coming from an investor's perspective, Behahani advised that biotech companies developing late-stage financing strategies should evaluate the expectations of potential partners, and try to "get crystallization" of those elements. "The last thing you want is to give up on your molecule. . . . Not everyone gets an M&A deal," Behahani said. "As long as [the deal] lets you live to fight another day, I think it's worth doing." ■

BIO 2011

Clearing Reimbursement Hurdle Requires Some Early Planning

By Mari Serebrov
Washington Editor

WASHINGTON – Even before overcoming the safety, efficacy and approval hurdles, biotechs should be looking ahead to the fourth hurdle – reimbursement.

“The race does not stop at regulatory approval,” Gil Beyen, chief business officer for TiGenix NV, said during a BIO International Convention panel on getting drug approval in a risk-averse world.

In fact, reimbursement can become one of the most challenging hurdles to overcome in the European Union (EU). While approval is a centralized process, reimbursement is determined by each member state, resulting in 27 different approaches.

For instance, pricing and reimbursement are considered one process in the UK, but they’re two separate processes in France, according to Bjorn Peters, business development director for Shire-Movetis NV, of Turnhout, Belgium. However, all the member states require comparative effectiveness and a budget impact analysis to determine reimbursement.

Choosing which member state to enter first takes some strategic planning that may be determined by market size or ease of reimbursement policy. “For both small and larger companies, it is a major effort,” Beyen said.

Leuven, Belgium-based TiGenix had the first cell-based therapy, ChondroCelest, approved in the EU in October 2009, but it is still in the middle of working out reimbursement with the various member states.

Shire’s Resolor also was approved in October 2009. Because of reimbursement policies, it was launched first in Germany and Belgium in January 2010 and then in the UK and Switzerland a few months later.

Part of the reimbursement challenge is that payers often want to see different endpoints than what regulators want. This can be frustrating when the payers question the approval decisions already made by regulatory authorities, including their efficacy and comparative effectiveness assessments, said Annie Hubert, director of European government and public affairs for Brussels-based Amgen Belgium.

Industry would like to see the EU reimbursement process simplified, Hubert said. Ideally, the benefit/risk profile should be evaluated on the pan-EU level and not be rehashed on the individual country level. Instead, reimbursement decisions should be focused on budget impact.

But until those changes are made, biotechs should prepare for the fourth hurdle as early as possible, the three panelists said. Then they can integrate the payer’s needs into their product development program. That integration would include payer endpoints, budget impact analysis,

target populations and the building of a logical rationale for a realistic price.

Overcoming the fourth hurdle is a growing issue, Hubert said, especially for start-ups that often see approval as their final goal. “We see the same thing happening in the U.S.,” she added, noting a greater emphasis on comparative effectiveness there.

But reimbursement is not the only issue facing biotechs as regulators become more risk averse. An increased focus on safety has led to a new EU pharmacovigilance directive that must be implemented in each member state by July 2012. Under that directive, biotechs must have a risk management plan for all new products and conduct post-authorization studies, Hubert said. ■

ADA 2011

MacroGenics is Optimistic on Posthoc Analyses of Protégé

By Anette Breindl
Science Editor

Among the data to be presented at the American Diabetes Association’s annual meeting this week were additional analyses of Rockville, Md.-based MacroGenics Inc.’s anti-CD3 antibody teplizumab.

Teplizumab failed to meet its primary endpoint of lowering insulin use and A1C levels in the phase III Protégé trial last year. (See *BioWorld Today*, Oct. 22, 2010.)

But MacroGenics CEO Scott Koenig remains optimistic about the drug’s prospects, saying that converging evidence on which populations the antibody would be most useful in, plus newer guidance on trial endpoints, could enable teplizumab to ultimately prevail.

The posthoc analyses, which were both presented at the ADA meeting and just published in *The Lancet*, suggested that teplizumab may have a better chance of meeting its endpoints in younger patients, as well as those who have been recently diagnosed.

“The most dramatic effect was in the children,” Koenig said – and not just in the Protégé trial. Another teplizumab study, the Abate trial, also found that its biggest effect appeared to be in 8-12 year olds.

Koenig said that the company will report the detailed data, and reach out to both the clinical community and regulatory agencies to get their input on how to proceed.

And, he told *BioWorld Today*, “obviously we have to do another clinical study . . . and we have to find a way to pay for such a study. All these are things we will be pursuing.”

Teplizumab targets the CD3 antibody, which is expressed on T cells; it works – or is supposed to – by slowing down the destruction of pancreatic islet cells by T cells. Teplizumab is not the only anti-CD3 antibody in

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Innovation

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Yet even biotech is going through its own forced pipeline prioritization, often choosing less risky programs because they are more likely to attract much-needed investments.

"Innovation comes out of diversity," noted Jit Patel, director of global discovery alliances at AstraZeneca plc. "And that diversity pool is shrinking."

He added that big pharma is looking more to academia, even suggesting that "we cut out the middleman of biotech."

But the world of academia is facing its own constraints,

pointed out panelist Tillman Gerngross, founder and CEO of antibody platform firm Adimab LLC.

While the NIH has implemented programs to help drug discovery, the agency is unwittingly hindering innovation, he added.

"NIH believes it's in the drug discovery business, and that's a really bad thing," he said. Instead, NIH should be funding the "really risky science."

Then it should be up to biotech, an industry far more nimble and entrepreneurial compared to its big pharma brethren, to foster that innovation. If successful, biotechs will be able to create value for their own investors as well as attract big pharma to the table.

And the good news is that big pharma still remains willing to pay for promising assets, though recent deals might not boast the inflated financial terms.

Wary after past failures with high-dollar early stage candidates, pharma is taking a more cautious approach, using creatively structured agreements such as earn-outs and terms that have "become a lot closer to reality," noted Jason Rhodes, executive vice president and chief business officer of epigenetics firm Epizyme Inc.

But small biotech can take advantage of pharma's caution in other ways.

Cambridge, Mass.-based Epizyme, for example, inked a potentially \$206 million deal in March with Eisai Co. Ltd. for preclinical lymphoma candidate EZH2.

The up-front payment was a modest \$6 million, but Eisai will fund all costs through Phase II, after which the small biotech has the option to go in 50-50 for the program in the U.S. (See *BioWorld Today*, March 11, 2011.)

"I think it's a very unusual term for an early stage deal," Rhodes said. But that opt-in component was the "keystone element."

Another positive trend is the number of large biotechs jumping into the in-licensing game, since those firms are suffering the same drop-off in R&D productivity as large pharma.

So there's definitely competition for innovative assets, said Steven Ertel, senior vice president of corporate development at Acceleron Pharma Inc. "It's just a different set of licensors." ■

Wondering What You Missed in *BioWorld Insight*?

No-Strings Deals Let Rivals Combine Unapproved Drugs

Science has taught us that many diseases – including HIV, HCV and cancer – can only be controlled by cocktails containing several drugs. Business has taught us that the best drugs don't necessarily come from your own pipeline, and they aren't always for sale. Hence the rise of no-money, no-rights, no-strings-attached deals to combine multiple unapproved drugs from multiple sponsors in a single clinical trial. *BioWorld Insight* explored the benefits and challenges of this new business development model.

Art of Spec Pharm Licensing: Balancing Risk & Innovation

Specialty pharma has often been associated with a risk-reduced business model. But recently, some spec pharma firms have been making gambles on high-risk, high-innovation technologies – such as United Therapeutics Corp.'s license of placental cell technology from Pluristem Ltd. *BioWorld Insight* explored spec pharma companies' moves toward and away from innovation, and what goes into their decisions when balancing risk and reward.

Into the Breach: Genentech Not Alone in Targeting BBB

Genentech Inc./Roche AG scientists recently made a splash by delivering antibodies across the blood-brain barrier, a 400-mile-long protective layer that lines the blood vessels of the brain. But they aren't the only ones making progress against what has long been a delivery headache for central nervous system drug developers.

Take *BioWorld Insight* for a test drive. Call (404) 262-5476 or (800) 688-2421 and mention editor Trista Morrison for a free trial subscription.

Other News To Note

- **Prana Biotechnology Ltd.**, of Melbourne, Australia, presented preclinical data indicating that PBT2, which is in Phase II for Alzheimer's disease, may also be applicable in Huntington's disease. The data were presented at the Huntington's Disease Society of America annual national convention. Phase II trials are being planned in both indications.

Biosimilars

Continued from page 1

application and other manufacturing-related information.

"Fundamentally, having to provide your entire application is very disturbing to the biosimilar applicant," Mark Bowditch, a patent attorney with Princeton, N.J.-based Sandoz Inc., said during a panel on biosimilar patent strategies at the BIO International Convention in Washington.

That step requires the biosimilar firm to disclose its most sensitive information to its "bitterest enemy" and most formidable competitor, Bowditch added. Given the other requirements of the pathway, it may be enough to have biosimilars wait until the patents expire.

Innovator companies are restricted as to who can see the disclosed confidential information. But the enforcement provisions are weak, Bowditch said. Besides, it's hard to undo the damage once it's been done.

The next step requires an exchange of patent lists. The innovator company begins this part of the waltz by giving the follow-on, within 60 days, a list of patents that could be infringed, identifying those patents it would be willing to license to the applicant.

The biosimilar firm then has 60 days to come up with

its own list of patents that could be infringed, along with a claim-by-claim analysis of the patents on both lists showing why they are invalid, unenforceable or not infringed, according to Edward Murray, counsel for Merck & Co. Inc., of Whitehouse Station, N.J.

The sponsor, in turn, gets 60 days to respond, giving reasons why each claim is valid, enforceable or infringed.

This part of the dance could affect future licensing agreements, especially those between biotechs and universities, said Bart Newland, vice president and chief intellectual property counsel for Biogen Idec Inc., of Weston, Mass.

Some licensors don't give companies the right to enforce the patent, which would restrict the exchange required in the biosimilar pathway.

Since many such agreements are already in place, Newland predicted, "It's going to get messy."

Universities too often focus on the revenue in their licensing agreements rather than the enforcement of the patent, Murray agreed. But going forward, biotechs will have to change the way they license from academia to address the interplay required by the biosimilar path.

"If I don't have the right to enforce, that really reduces the value of the license," Murray said. ■

ADA

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the works; Swiss Biotech NovImmune SA and Tolerx Inc. of Cambridge, Mass., also have anti-CD3 antibodies in development. Earlier this year, Tolerx Inc. failed in Phase III with its oteelixizumab. (See *BioWorld Today*, March 14, 2011)

Koenig said that in his opinion, two failed trials do not add up to a wrong target. Oteelixizumab, he said, was given at a much lower dose in the Phase III trial than in earlier studies. Teplizumab, too, was "much more effective" at the highest dose tested than at lower doses.

"We don't think this is a class effect," he said, "though we obviously have to design the right trial to prove that."

In other news from the conference:

- **Arcion Therapeutics Inc.**, of Baltimore, reported results of its topical clonidine gel for patients with diabetic neuropathy. In patients with diabetic neuropathy who were still relatively sensitive to painful stimuli, 12 weeks of treatment with 0.1 percent topical clonidine gel applied three times daily to the feet decreased their mean pain level relative to placebo. In patients with less initial sensitivity to pain there was no significant effect.

- **ChemoCentryx Inc.**, of Mountain View, Calif., reported preclinical data on its CCR2 antagonist CCX140. In two mouse models of diabetes, treatment with CCX140 significantly improved multiple metabolic and renal parameters including hyperglycemia, insulin sensitivity and markers of kidney function. CCX140 is in clinical development, and the company plans to start a Phase

II trial with the compound for the treatment of diabetic nephropathy.

- **DARA BioSciences Inc.**, of Raleigh, N.C., presented safety and pharmacokinetic results from a Phase I trial of its dual PPAR delta/gamma agonist DB959. The company said those results provided support for the continued clinical development of DB959, and that a second clinical study is nearing completion with results expected to be available during Q3.

- **Diamyd Medical AB**, of Stockholm, Sweden, reported detailed results from the company's European Phase III study of its diabetes immunotherapy Diamyd. Pre-specified subgroup analyses suggested that Diamyd had an effect in several subgroups. In particular, male study participants treated with Diamyd had significantly higher levels of C-peptide than those receiving placebo. Diamyd reported last month that the study missed its primary endpoint. (See *BioWorld Today*, May 10, 2011.)

- **Intarcia Therapeutics Inc.**, of Hayward, Calif., presented 48-week results from a Phase II study on its ITCA 650 (DUROS subcutaneous continuous delivery of exenatide). Patients experienced reductions in A1C, fasting plasma glucose, and body weight during the 48 weeks of treatment at all doses tested. The study enrolled 155 Type II diabetes patients.

- **Takeda Pharmaceutical Co. Ltd.**, of Osaka, Japan, presented data from a Phase II randomized, double-blind, placebo- and comparator-controlled, parallel-group,

See ADA, Page 10

Avastin

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drug for metastatic breast cancer while Genentech pursues new studies to support Avastin's use in the indication.

Presiding officer Karen Midthun, director of the Center for Biologics Evaluation and Research, mitigated any drama on the outcome of the two-day meeting at the outset. Although the panel will vote Wednesday afternoon, she said, the final decision on the fate of Avastin for metastatic breast cancer will rest with FDA Commissioner Margaret Hamburg. Midthun also revealed that the agency will keep the public docket open for comments and for a final submission by CDER and Genentech until July 28 – two weeks longer than initially indicated.

Perhaps seeking to blunt public criticism about the decision to reject a request from FDA colleagues to require outside scientific experts to disclose financial ties to Genentech or other manufacturers, Michael Ortwerth, director of the Advisory Committee Oversight and Management Staff in the FDA's Office of Special Medical Programs, stated for the record that members of the committee were screened for potential conflicts of interest and no waivers needed to be issued with respect to the hearing.

Most – but not all – of the speakers who subsequently made three-minute statements supported continued availability of Avastin for metastatic breast cancer. In addition to patients and oncologists, representatives from several advocacy organizations outside the breast cancer arena worried aloud that the agency's proposal to remove the labeling for Avastin in metastatic breast cancer might represent the first in a series of dominos that could lead to the withdrawal of the drug for other approved treatments, including those for advanced colon, lung and kidney cancers.

A handful also commented on what seem to be among the two biggest questions: How will the FDA's decision, either way, reflect on the future of the accelerated approval process? And how will the uncertainty about the FDA's decision-making process affect future drug development?

Using hundreds of slides, CDER officials spent the next two hours laying their case, citing legal, scientific and public policy issues.

"While CDER and Genentech disagree about many issues to be discussed today, one issue about which there is no dispute is that Avastin has not been demonstrated to improve overall survival in patients with metastatic breast cancer in clinical trials," Richard Pazdur, director of CDER's Office of Oncology Drug Products, told the panel.

For their part, Genentech officials sought to find common ground with CDER on its evaluation of safety and efficacy, walking panelists through the company's own dataset and asking for confirmation of their findings. In often testy exchanges, company and federal officials sparred about differences on dosages, patient quality of

life, hazard ratios, response rates, trial design, variations in data by chemotherapy arms and median differences in progression-free survival (PFS).

On that final point, testimony during day one suggested the FDA may seek to close the PFS door the agency opened in February 2008 with the accelerated approval of Avastin. (See *BioWorld Insight*, March 3, 2008, and *BioWorld Today*, Feb. 25, 2008.)

In fact, Pazdur suggested as much, stating, "an improvement in overall survival of a given magnitude has a clearer meaning in a benefit-risk analysis than the same magnitude of improvement in PFS.

"CDER has consistently emphasized that a demonstration of a statistically significant improvement in PFS may not translate to a favorable benefit-risk decision," he added. ■

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multicenter study, which was conducted to evaluate the efficacy, safety and tolerability of once-daily treatment with five different doses of TAK-875 in Type II diabetes patients over 12 weeks. Compared to placebo, all doses of TAK-875 showed significantly greater A1C reductions at week 12. TAK-875 is a selective agonist of GPR40, one of the G-protein-coupled receptors on pancreatic islet cells.

• **Zealand Pharma A/S**, of Copenhagen, Denmark, presented new preclinical data on ZP2929 in disease models for diabetes and obesity. ZP2929, a glucagon/GLP-1 dual agonist in combination with long-acting insulin caused a greater loss in body weight and fat mass as compared to treatment with liraglutide. ■

Clinic Roundup

• **Anlylam Pharmaceuticals Inc.**, of Cambridge, Mass., presented new data from its ALN-TTR program at the 2011 Peripheral Nerve Society Meeting in Potomac, Md. The company reported results from a natural history study designed to measure blood levels of wild-type and mutant transthyretin over time in both transthyretin-mediated amyloidosis patients and gene carriers. The study enrolled 26 patients and gene carriers with seven amyloidogenic TTR mutations, the most common being the Val30Met mutation that is the primary cause of familial amyloidotic polyneuropathy. Data from the study showed that TTR levels were stable over time in patients and carriers. Anlylam scientists and collaborators also presented preclinical data from its ALN-TTR program, including new data demonstrating improved potency with ALN-TTR01 using a loading dose/maintenance dose regimen. ALN-TTR01 is currently in a Phase I trial for the treatment of ATTR.

Financings Roundup

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(See *BioWorld Today*, Aug. 10, 2009.)

All of Acetylon's Series A investors participated in the Series B round, but with an average investment of just \$1 million, the biotech had to attract many new investors as well. Ogier said it all came down to networking – “people reaching out to people that they knew” – and substantial support from the board of directors. Acetylon was also helped by the reputation and connections of its scientific founders, Harvard University researcher and serial entrepreneur Stuart Schreiber and Dana-Farber Cancer Institute researcher Kenneth Anderson.

Proceeds will predominantly be used to advance HDAC6 inhibitor ACY-1215 into Phase I/II trials for multiple myeloma. Investigational review board approvals for the trial are under way and Ogier expects enrollment to begin this summer.

HDACs are a hot target in the cancer field, but their potency has thus far come hand in hand with serious side effects.

Merck & Co. Inc.'s HDAC inhibitor Zolanza (vorinostat) is approved for recurrent cutaneous T-cell lymphoma (CTCL) but has warnings for pulmonary embolism, thrombocytopenia and gastrointestinal disturbances, among other side effects. Celgene Corp.'s HDAC inhibitor Istodax (romidepsin) is approved for CTCL and peripheral T-cell lymphoma (PTCL), but it also carries many warnings – among them thrombocytopenia, leucopenia, anemia, severe infections, tumor lysis syndrome and electrocardiographic changes.

The problem, Ogier explained, is that Zolanza and Istodax are pan-HDAC inhibitors, unable to distinguish between the 18 enzymes in the HDAC family. Ditto for belinostat, which Spectrum Pharmaceuticals Inc. is advancing through a pivotal trial for PTCL.

“The effectiveness of these drugs is not controversial,” Ogier said. “The activity is there,” but the significant side effects make pan-HDAC inhibitors difficult to combine with other cancer drugs and difficult to extend into less serious indications.

Hence Acetylon's focus on isoform-selective HDAC inhibitors. Lead compound ACY-1215 targets HDAC6, which disrupts a cell's ability to dispose of damaged proteins, leading to a buildup of trash that triggers apoptosis of the diseased cell.

Ogier said Acetylon is “very excited” about ACY-1215's preclinical profile and potential to avoid the side effects associated with pan-HDAC inhibitors. The Leukemia & Lymphoma Society is excited, too – the nonprofit is contributing \$4.85 million, separate from the Series B financing, to support the Phase I/II multiple myeloma trial.

Beyond the lead program, Ogier said Acetylon is working with several academic investigators to explore the potential of ACY-1215 in lymphoma, leukemia and solid tumors.

Additionally, the biotech is in late preclinical development with a second HDAC6 inhibitor for autoimmune diseases such as rheumatoid arthritis and Crohn's disease. Ogier said that program has attracted partnering interest.

Earlier in its pipeline, Acetylon is investigating the use of selective HDAC inhibitors in neurodegenerative diseases and infectious diseases.

Other biotechs, too, are beginning to address the safety issues of pan-HDAC inhibitors. In April, 4SC AG inked a Japanese deal for its pan-HDAC inhibitor resminostat, which it said is designed to have a better safety profile than existing compounds. Meanwhile Karus Therapeutics Ltd. has a discovery program focused on HDAC6 inhibitors.

(Editor's note: Ogier and others will be discussing the changing role of VCs in funding innovation and the new normal for start-up biotechs during BIO 2011 today at 10 a.m. in Room 149AB. Don't miss it!)

In other financing news:

- **Achillion Pharmaceuticals Inc.**, of New Haven, Conn., closed its previously announced \$65.1 million public stock offering. The company sold 11.04 million shares, including full exercise of the over-allotment option, for \$5.90 apiece. Net proceeds of \$60.9 million will be used to advance clinical trials of several antiviral candidates for treatment of chronic hepatitis C virus, including ACH-1625, ACH-2684 and ACH-2928. (See *BioWorld Today*, June 23, 2011.)

- **Amgen Inc.**, of Thousand Oaks, Calif., sold \$750 million worth of 2.3 percent senior notes due 2016, \$1 billion worth of 4.1 percent senior notes due 2021 and \$1.25 billion worth of 5.65 percent senior notes due 2042. The \$3 billion in debt will be used for general corporate purposes, including share repurchases and quarterly dividend payments.

- **Nimbus Discovery LLC**, of Cambridge, Mass., raised \$24 million in Series A financing. The round was co-led by Atlas Venture, SR One and Lilly Ventures, and it included participation by existing investor Bill Gates. Proceeds will be used to accelerate existing programs targeting IRAK4 and ACC in inflammation, cancer and metabolic disease and to use its computational drug discovery platform to expand its pipeline. (See *BioWorld Today*, March 28, 2011.) ■

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Other News To Note

- **Progenics Pharmaceuticals Inc.**, of Tarrytown, N.Y., submitted a supplemental new drug application to the FDA for approval of Relistor (methylnaltrexone bromide) subcutaneous injection for the treatment of opioid-induced constipation (OIC) in patients with chronic, noncancer pain. Relistor is approved and sold in the U.S., EU, Canada, Australia and other countries for the treatment of OIC in patients with advanced illness who are receiving palliative care when response to laxative therapy has not been sufficient.

- **RESprotect GmbH**, of Dresden, Germany, received back North America rights for RPI01, the company's anticancer drug, from its former North American partner, **SciClone Pharmaceuticals Inc.**, of Foster City, Calif. In 2009, SciClone discontinued a Phase II trial of RPI01, a nucleoside analogue, in late-stage pancreatic cancer. RESprotect said it gained approval from German authorities for an adapted development plan for RPI01, enabling development of the compound to be reinitiated this year. The company plans to proceed into a pivotal Phase IIb study for late-stage pancreatic cancer and said German authorities have indicated the study could be sufficient to file for marketing authorization in the European Union.

- **Shire plc**, of Dublin, Ireland, completed its \$750 million cash acquisition of **Advanced BioHealing Inc.**, of Westport, Conn. The Advanced BioHealing business becomes part of Shire's specialty pharmaceuticals business and will leverage biologic manufacturing expertise from Shire's human genetic therapies business. Kevin Rakin, CEO of Advanced BioHealing, will continue to lead the business within the Shire organization. (See *BioWorld Today*, May 19, 2011.)

- **Theratechnologies Inc.**, of Montreal, reported that the marketing authorization application (MAA) for tesamorelin submitted by its partner, **Ferrer Internacional SA**, of Barcelona, Spain, was accepted for review by the European Medicines Agency. The MAA is based on positive results from two Phase III trials that enrolled more than 800 patients and follows tesamorelin's marketing approval by the FDA in November 2010 under the trade name Egrifta. Tesamorelin is designed to treat HIV-associated lipodystrophy, a metabolic complication that affects patients taking antiretroviral therapies long term. Ferrer holds the commercialization rights to tesamorelin for the treatment of excess abdominal fat in adult HIV-infected patients with lipodystrophy in Europe and is responsible for conducting related regulatory and commercialization activities. (See *BioWorld Today*, Nov. 12, 2010.)

- **Uluru Inc.**, of Addison, Texas, approved a 15-for-1 reverse stock split of the company's common stock, effective today. The company filed an amendment to its

restated articles of incorporation to effect the reverse stock split, which was authorized by stockholders at ULURU's reconvened annual meeting on June 16. Following the reverse stock split, the company expects to have approximately 5.8 million shares of common stock outstanding.

Clinic Roundup

- **Anacor Pharmaceuticals Inc.**, of Palo Alto, Calif., reported preliminary results from its Phase IIb trial of AN2728 for the treatment of mild-to-moderate plaque-type psoriasis. The trial enrolled 68 subjects randomized in a 2:1 ratio, AN2728 to vehicle. Subjects treated with AN2728 showed improvement over vehicle at each of the recorded timepoints during the 12-week study period with peak efficacy of 26 percent occurring after six weeks of treatment with AN2728. The Phase IIb trial, while not powered to demonstrate statistical significance, was conducted under anticipated Phase III conditions.

- **BCO Pharma Ltd.**, of County Cork, Ireland, said it plans to conduct a Phase III trial, through affiliate BrePco Biopharma Ltd., of its lead product – a novel form of dopamine, the most commonly used inotropic agent in premature babies who require treatment for hypotension. About 2 percent to 3 percent of newborns and infants experience potentially life-threatening hypotension, but current treatment regimens use drug formulations that were developed for and primarily studied in adults. The Phase III study is aimed at bringing to market a more appropriate and safer formulation for infants. Subject to approval by the European Medicines Agency, initial dosing is expected to commence this fall.

- **BioLineRx Ltd.**, of Jerusalem, enrolled the first patient in the Phase II/III CLARITY trial of BL-1020, a first-in-class, orally available, GABA-enhanced antipsychotic for the treatment of schizophrenia. The CLARITY trial is designed as a randomized, double-blind, placebo-controlled study and is expected to be conducted in 15 sites in Romania and 19 sites in India, enrolling 435 patients with acute exacerbation of schizophrenia. The primary endpoints are short-term cognitive benefit and anti-psychotic efficacy, safety and tolerability in schizophrenia patients over a six-week period compared with risperidone and placebo. Determination of the long-term effects of the drug, over a period of 24 weeks, is a secondary endpoint. The company expects to report results from the CLARITY trial in the fourth quarter of 2012.

- **Celladon Corp.**, of La Jolla, Calif., said data from its completed Phase II CUPID study of Mydicar, an enzyme replacement therapy, for advanced heart failure is being published online in *Circulation*. Previously announced top-line results of 39 patients met the study's primary safety and efficacy endpoints at six months for high-dose Mydicar compared to placebo.

Clinic Roundup

- **Morphotek Inc.**, of Exton, Pa, has commenced a randomized, double-blind, placebo-controlled multicenter Phase II study of farletuzumab in adenocarcinoma of the lung. The study will evaluate whether farletuzumab, a monoclonal antibody, delays the time to tumor progression when it is added to one of the standard-of-care chemotherapy options for metastatic adenocarcinoma of the lung. It will enroll up to 120 patients. As part of the study, a diagnostic test for the antibody's target, folate receptor alpha, will be used to determine patient eligibility.

- **Palatin Technologies Inc.**, of Cranbury, N.J., said that enrollment of patients has commenced in its Phase IIb clinical trial evaluating the efficacy and safety of bremelanotide (PT-141), a melanocortin agonist being developed for the treatment of female sexual dysfunction. The multicenter, placebo-controlled, randomized, parallel group trial will test three dose levels of subcutaneously administered bremelanotide in 400 premenopausal women.

- **Relypsa Inc.**, of Santa Clara, Calif., initiated a Phase IIb trial of RLY5016 for the treatment of hyperkalemia in

patients with diabetic nephropathy and chronic kidney disease. The AMETHYST-DN trial will evaluate the safety and efficacy of RLY5016 in reducing high potassium levels in patients with moderate to severe kidney impairment who are being treated with renin-angiotensin-aldosterone-system (RAAS) inhibitors.

- **Sanofi SA** subsidiary Genzyme Corp., of Cambridge, Mass., and **Isis Pharmaceuticals Inc.**, of Carlsbad, Calif., said that additional analyses from Phase III studies of statin add-on mipomersen for heterozygous familial hypercholesterolemia (heFH) were presented at the 79th European Atherosclerosis Society Congress. Those analyses showed that mipomersen reduced the levels of the atherogenic lipoproteins Lp(a) and LDL-C. Data from the trials were first released last year. (See *BioWorld Today*, Feb. 11, 2010.)

- **Sinovac Biotech Ltd.**, of Beijing, has entered into a Phase II trial with its EV71 vaccine for human enterovirus 71 (EV71), the virus that causes hand, foot, and mouth disease. The Phase II trial is a single-center, randomized, double-blinded and placebo-controlled study evaluating 540 healthy volunteers from 3 to 35 months of age to determine the optimal vaccine dose. The company had announced positive Phase I results in May.

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