COMMON SENSE

GSK strikes $1.5 billion-plus deal to use Isis’ antisense platform for development of rare disease therapeutics
BY AMY SWIDERMAN
CARLSBAD, Calif. — Seeking to further its concentration on the promising research area of rare and severe disease, London-based pharma GlaxoSmithKline PLC (GSK) announced in late March a blockbuster deal with Isis Pharmaceuticals, a drug developer known for its expertise in RNA-targeted therapeutics, that will apply Isis’ antisense drug discovery platform to seek out and develop new therapeutics against targets for infectious diseases and some conditions causing blindness.

Under the terms of the agreement, which covers up to six programs, Isis will receive an upfront $35 million payment from GSK and is eligible to receive up to $20 million in milestones per program up to Phase II proof-of-concept (PoC). GSK will have the option to license compounds at PoC, and will be responsible for all further development and commercialization. Should all six programs be successfully developed for one or more indications and commercialized through to pre-agreed sales targets, Isis continued on page 31

An ironclad partnership
AMAG and Takeda announce strategic collaboration for iron deficiency anemia drug Feraheme
BY JEFFREY BOULEY
LEXINGTON, Mass. — AMAG Pharmaceuticals Inc. and Osaka, Japan-based Takeda Pharmaceutical Co. have entered into a license, development and commercialization agreement related to Feraheme (ferumoxytol) injection for intravenous (IV) use in all therapeutic indications.

Feraheme is already indicated for the treatment of iron deficiency anemia in adult patients with chronic kidney disease. But looking to the rest of this year, AMAG is keen to advance its clinical development programs for the treatment of iron deficiency anemia in other indications as well. For example, Feraheme shows promise for treating iron deficiency anemia in women with abnormal uterine bleeding and in patients with cancer and gastrointestinal diseases.

Feraheme is also being developed as a diagnostic agent for vascular-enhanced magnetic resonance imaging. AMAG notes AMAG continued on page 10

Patent wars persist
Myriad poised to appeal court ruling invalidating patents on breast cancer genes
BY LORI LESKNO
NEW YORK— A federal court ruling invalidating patents on the breast cancer genes BRCA1 and BRCA2, held by Myriad Genetics Inc., has sent shock waves through the biotech community, industry stockholders, investors and patent attorneys. But the controversial decision rendered by New York Federal District Judge Robert W. Sweet on March 29 could just be the beginning.

Attorneys for the American Civil Liberties Union argued that patents on human genes violate the First Amendment and patent law because genes are “of nature.” ACLU continued on page 38

SHOW PREVIEW: The American Society for Microbiology
heads to sunny San Diego for its 110th General Meeting
SEE PAGE 18

WINNERS AND LOSERS IN HEALTHCARE REFORM: New legislation has pros and cons for pharmaceutical industry
SEE PAGE 37
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Achaogen to use $56 million Series C financing to advance antibiotics program

SAN FRANCISCO—Achaogen, a biopharmaceutical company focused on the discovery and development of innovative broad-spectrum antibiotics to treat life-threatening, multi-drug resistant (MDR) bacterial infections, announced in April the completion of a $56 million Series C round of financing.

Dr. Kevin Judice, CEO and chief scientific officer of Achaogen, said the financing round, together with non-dilutive capital that the company has secured through partnerships with various government agencies, will enable Achaogen to advance multiple clinical programs, including conducting a Phase II study in complicated urinary tract infections of ACHN-490, Achaogen’s lead candidate for multi-drug resistant bacterial infections.

ACHN-490 has demonstrated a positive safety and dosing profile in Phase I clinical testing and displayed broad spectrum efficacy in preclinical studies against systemic infections caused by MDR Gram-negative bacteria (e.g., E. coli, K. pneumoniae and P. aeruginosa) and MRSA. In addition, the company is pursuing preclinical programs in several other areas of interest to combat the global emergence of bacterial resistance and developing next-generation aminoglycosides called “neoglycosides.” Achaogen’s lead neoglycosides display broad-spectrum activity against many resistant bacteria that cause systemic infections, including K. pneumoniae, E. coli and MRSA.

“Achaogen combines excellent science with a compelling business model, blending venture capital and non-dilutive financing to advance multiple programs that have potential to address the increasing dire need for new agents to treat multi-drug resistant bacteria worldwide,” says Robert More, general partner of Frazier Healthcare, a new investor that led the financing round. In conjunction with the financing, More will join the Achaogen board of directors.

Boehringer Ingelheim launches life sciences venture capital fund

INGELHEIM, Germany—Boehringer Ingelheim in late March announced the launch of the Boehringer Ingelheim Venture Fund (BIVF) to create a corporate venture capital fund that aims to invest in biotech and start-up companies that provide “groundbreaking therapeutic approaches and technologies to help drive innovation in medical science.”

Boehringer Ingelheim has initially committed to invest a total fund volume of nearly €136 million, with the first investments being made this year. Investment opportunities will be sought on a worldwide basis.

According to the German pharma, these approaches and technologies may include—but are not limited to—new therapeutic concepts including stem cells and RNA silencing as well as new-generation vaccines, protein or antibody technologies, new molecular targets and/or first-in-class lead compounds. Disease-related biomarkers would be an additional area of focus.

“We are aware that there is an entire landscape of novel therapeutic ideas and potentially breakthrough technologies that need to be supported for future patients’ benefit,” says Prof. Andreas Barner, chairman of the company’s board of managing directors.

Parties interested in contacting the BIVF should visit www.boehringer-ingelheim-venture.com. ddn

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**Pharmaceutical and Biotech Market Indices**

**Amex Pharmaceutical Index**

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**Biotech posts strong first quarter gain**

SAN FRANCISCO—Biotech racked up impressive gains for both the month of March and the first quarter of 2010, benefiting from robust general markets this quarter and the passage of healthcare reform legislation in March, according to venture capital firm Burrill & Co.

Regarding the latter contributing factor, G. Steven Burrill, CEO of the firm, says, “While investors initially gravitated to investing in Medicaid insurers and HMOs in the wake of the passage of the healthcare reform bill, the prospect of adding millions of new paying patients certainly is a plus for pharma and biotech companies.”

Shares of Amylin Pharmaceuticals were up 19 percent in March and 58.5 percent for the quarter after the U.S. Food and Drug Administration (FDA) did not ask the company and its partners Eli Lilly & Co. and Alkermes to conduct additional studies on the drug Bydureon, a once-weekly version of the twice-daily Byetta injection. Illumina’s shares jumped 23 percent for the month and 26.5 percent for the quarter after the company received favorable publicity after sequencing of the genome of actress Glenn Close.

Genzyme’s shares were off 9.4 percent in March following the company’s announcement that the FDA planned to enforce plant operation inspections at its Boston facility, and Myriad Genetics Inc., whose shares also slipped after a court overturned a group of patents on gene sequences linked to breast cancer and ovarian cancer, which Myriad uses in tests for those diseases.

While venture capital continued to flow to U.S. biotech companies, it was in short supply for public companies, Burrill says. Approximately $1.044 billion of venture capital was invested in the first quarter of 2010, an increase of 7 percent over the prior quarter. However, follow-on financing fell 32 percent and only PIPE financing showed a slight increase in the amounts raised compared to the previous quarter.

“The total of $2.9 billion raised in the first quarter of this year was down almost 32 percent from the Q1 ’09 total. This points to the fact that while the capital markets have improved, and big biotechs have benefited from this, the environment for raising capital still remains soft,” adds Burrill. “Investors are not yet ready to participate fully in the risks associated with developmental stage biotech companies. Even though three biotech IPOs managed to get out this quarter interest in them was at best lukewarm.”

**Roche sales up 6 percent in first quarter**

BASEL, Switzerland—Roche Holding AG reported a 6 percent increase in first-quarter sales and said its strong performance was owed to sales of its anti-cancer drugs such as Avastin and Rituxan. Sales grew to $11.6 billion from $10.9 billion in the first three months of 2009. Sales of Avastin and Rituxan rose 18 percent and 13 percent, respectively. Roche’s third billion-dollar anti-cancer drug, Herceptin, sold 11 percent more during the quarter. Sales of Tamiflu also rose 32 percent during the tail end of the northern hemispheric’s flu season. Year-ago sales of Tamiflu were unaffected by the swine flu outbreak, which occurred in the second quarter of 2009. Roche said its diagnostics division also increased sales by 7 percent to $2.4 billion.

**MDRNA down to $1.7 million in cash**

BOTHELL, Wash.—RNAi-based drug developer MDRNA Inc. said in its fourth-quarter financial report that it just had $1.7 million of cash and investments left in the bank heading into 2010, about half as much as the company had at the same time a year earlier. With no marketed products generating revenue, the company reported a net loss of about $800,000 in Q4 2009. Based on the lack of available cash, MDRNA said its auditing firm, KPMG, is likely to issue an opinion in the company’s annual report that raises doubt about its ability to continue as a “going concern.” The company also reported a Q4 loss of 2 cents per share, narrower than the year-ago loss of 39 cents per share. Revenue was $200,000, flat with year-ago levels.

**Generic drugmaker Mylan sees profit in Q4**

CANONSBURG, Pa.—Mylan Inc. reported fourth-quarter profits of $4.1 million, or 1 cent per share, a turnaround from a loss of $54.6 million, or 18 cents, in the final three months of 2008. Fourth-quarter revenue rose 12 percent to $1.35 billion from $1.2 billion, aided by a weaker U.S. dollar. For the full year, Mylan posted net income of $93.5 million, up from a loss of $335.1 million in 2008. Revenue decreased to $5.09 billion from $5.14 billion a year earlier, while revenue from generics increased to $4.70 billion from $4.29 billion. Mylan said it recorded unfavorable litigation charges of $114.2 million in the most recent quarter stemming from a settlement to resolve pricing claims. Excluding those charges and other special items, the company earned 33 cents per share, in line with Wall Street estimates.
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sanofi-aventis inks diabetes test agreement with AgaMatrix

BY LORI LESKO

PARIS—Strengthening its position in the growing global diabetes market, sanofi-aventis has signed a long-term agreement with Salem, N.H.-based AgaMatrix for the development, supply and commercialization of blood glucose monitoring (BGM) tests.

The products developed will be aimed at reducing the perceived complexity of managing patients on insulin therapy. Starting in the second half of 2010, sanofi-aventis plans to commercialize the first products of this partnership, capitalizing on the company’s expertise with insulin and insulin delivery, and building on AgaMatrix’s advanced technology and BGM development capabilities.

The agreement calls for sanofi-aventis to combine its brands, Lantus, a basal insulin, and Apidra, a fast-acting insulin, with AgaMatrix’s blood glucose monitors (BGMs). Under terms of the deal, sanofi-aventis will hold exclusive licenses to the BGMs that are co-developed by the two companies and will sell through its Global Diabetic Division. AgaMatrix may continue to commercialize its own BGMs, separately from the deal.

Pierre Chancel, head of sanofi-aventis’ diabetes division, referred to the agreement in a statement as a “concrete step towards fulfilling our vision to deliver integrated solutions to patients and become the partner of choice in the field of diabetes.” sanofi-aventis CEO Christopher Viehbacher mapped out a strategic last year of reducing the company’s reliance on branded prescription drugs and diversifying. At the same time, Viehbacher expressed an interest in certain areas of medical technology, including devices that allow patients to measure their health at home, according to Reuters.

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EXPRESSING THEMSELVES

Eden Biodesign brings its cGMP manufacturing expertise together with Millipore’s UCOE express technology

BY JEFFREY BOULEY

LIVERPOOL, England—Eden Biodesign Ltd. and Billerica, Mass.-based Millipore Corp. have announced a partnership that will provide biopharmaceutical companies with access to what they call “a powerful combination of Eden’s cGMP manufacturing and Millipore’s Ubiquitous Chromatin Opening Elements (UCOE) expression technology.” As part of the agreement, Eden Biodesign will employ Millipore’s proprietary UCOE expression technology to undertake mammalian cell line development projects and cGMP production for third-party clients.

Dr. Roger Lias, president of Eden Biodesign’s North American subsidiary, says he looks forward to working with “a recognized industry leader like Millipore to make this extremely valuable technology available to our clients around the world.”

He adds that it is a vitally important consideration for his company’s clients that Eden address issues like speed-to-clinic, and the UCOE technology will help make that possible. Another critical consideration for clients, he says, is the ability to rapidly develop “highly productive cell lines that will support economically viable production through clinical development, process scale-up and steady-state large scale commercial supply.”

Millipore’s UCOE technology is able to notably improve on the process of gene expression for stably transfected mammalian cells by exerting effects on the structure of chromatin. According to Dr. Andrew Bulpin, vice president of upstream processing for Millipore’s Bioprocess Division, cells developed using Millipore’s UCOE technology are stable “high expressors.”

What that means, he notes, is that it is much easier and faster for biopharmaceutical manufacturers to identify high-yielding clones with the productivity and stability required for biomanufacturing than with many other expression systems.

Among the advantages of the UCOE technology is that more than 50 percent of UCOE-derived clones have higher expression than the best non-UCOE-derived clones, according to Millipore, and UCOE-derived vectors produce substantially more expressing clones than non-UCOE-derived vectors.

Reportedly, cell lines produced with UCOE technology are stable over 130 generations and high-yielding cell lines can be derived in less than 60 days without amplification. Users can also employ the technology to make two protein chains per plasmid—antibodies, for example—and users can express antibodies, receptors, enzymes, cytokines and more.

According to Millipore, the UCOE-induced productivity and stability of individual cells allows pools to be a source for rapidly generating gram quantities of proteins in three to four weeks. This offers potential advantages over transient transfection, as it minimizes the quantities of DNA and costly transfection agents. It also allows aliquots of the pool to be stored for future use if the protein is required at a later stage.

“Millipore is committed to bringing innovation that solves critical biopharmaceutical manufacturing business needs. Our distinctive UCOE technology, with its high expression elements, revolutionizes the speed by which protein therapeutics can be produced in mammalian cells,” Bulpin says, adding that he has “high expectations for the ongoing success of this partnership.”

Eden Biodesign Ltd.

Eden Biodesign’s production facilities feature three segregated clean room suites which in combination provide the capacity to manufacture mammalian, microbial and viral technologies for the production of natural or recombinant proteins, whole cells or virus products.

For more information, contact us at 919.653.5532 or visit our website at www.gentris.com
sanofi-aventis announces plans to expand operations in France

PARIS—Setting a goal for the company to change its chemical industrial activities in France to biotechnology and vaccine production by 2014, sanofi-aventis announced in late March that it will invest $201 million in its industrial plants, including $121 million for the creation of a new biosynthetic process in the industrial plants in Saint-Aubin-Lès-Etbeuf in Seine-Maritime and Vertolaye in Puy de Dôme, France. sanofi-aventis has been working on this goal since 2008, and since then, the company has devoted $938 million in that investment.

sanofi-aventis’ new plan also include a gradual phase-out of the facilities in Romainville in Seine-Saint Denis by the end of 2013, accompanied by a job stimulus plan to be implemented in the area. sanofi-aventis said the project also prepares the facilities for a decline in production that will follow patent expirations of several major drugs derived by synthetic chemistry.

Some new activities from Sanofi Pasteur would be housed in a new facility in Neuville-sur-Saline, Rhône, where a new vaccine against the dengue fever is slated for production. By 2014, this plant will become sanofi-aventis’ third-largest European center fully dedicated to vaccines.

The project will also includes measures to assist employees’ geographic mobility, especially in the Paris and Lyon area labor basins, and to facilitate career mobility by means of biotechnology training programs for 700 employees, to be implemented in partnership with French universities. ddn

Further reading:

- “It opens every large market in the world, whereas we are primarily focused on the U.S. and Europe,” he says. “The category is in excess of $6 billion on a worldwide basis with tens of millions of folks testing—and many more that are not yet testing or diagnosed. So the opportunity is very large.” ddn

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AZ continued from page 6

market authorizations for 18 products in nine countries.

“The agreement allows AstraZeneca to add further products and new countries where we see opportunities for growth, so we could potentially continue to buy licenses and market authorizations for additional products in additional countries, and pay Torrent for the supply of those products,” Sampson notes. The exact products and countries covered in the agreement are being kept confidential, as are financial terms.

“Assuming we commercialize these successfully, we believe we can broaden our portfolio of medicines not originated by AstraZeneca over time,” Sampson adds.

Torrent will manufacture the medicines working to AZ’s rigorous quality and process standards. Based in India, Torrent has been manufacturing medicines for more than 30 years and has a strong track record in registering and manufacturing a wide range of products.

“In markets where consumers and physicians have a strong preference for trusted brands, we believe AstraZeneca’s long-standing reputation for quality is a sustainable competitive advantage,” says Tony Zook, head of AZ’s global commercial organization.

“Working in partnership with Torrent will extend the range of branded medicines we can offer to patients in emerging markets, where we see continuing opportunities for our business to grow.”

The emerging markets are forecast to contribute around 70 percent of pharmaceutical industry growth in the next five years, and branded generics represent approximately 50 percent by value in these emerging markets. AZ believes it can capitalize on this opportunity and over time plans to broaden its portfolio beyond the initial 18 products.

“In total, we have identified an initial portfolio of about 100 molecules that we would like to be providing in these markets (not necessarily all from Torrent),” Sampson notes. “Not entirely surprisingly, these molecules are in therapeutic areas where we already have significant experience. This broadening of our portfolio allows us to leverage our commercial infrastructure and physician relationships, especially where we have a strong reputation and where doctors particularly value the high quality that we offer. And in some cases, having a branded generic can strengthen our position in tenders by allowing us to create differentiated offerings.”

While AZ hasn’t disclosed specific markets where its branded generics products will be sold, there is a role for branded generics in many of the emerging markets.

“Our broader emerging markets strategy includes continuing to grow in the large ‘BRIC-MT’ markets (Brazil, Russia, India, China, Mexico, Turkey),” Sampson says. But we also aim to extend our reach in high-growth small and mid-sized markets. We’ve acknowledged that BRIC-MT only represents 50 percent of the emerging market pharma opportunity, so the other half is in small and mid-sized markets. Ultimately, we believe branded generics will constitute 10 to 15 percent of our business in emerging markets.”

AMAG continued from page 1

that there are currently no iron-based vascular contrast agents approved for MRI in the United States, and the currently approved contrast agents used for MRI in the United States are all gadolinium-based—and thus associated with rare but severe adverse events in patients with chronic kidney disease. The initial focus of AMAG’s clinical development of Feraheme as an imaging agent is in assessing patients with peripheral arterial disease.

“One of our primary goals is to expand the reach of Feraheme to patients around the world with iron deficiency anemia,” says Dr. Brian J.G. Pereira, president and CEO of AMAG Pharmaceuticals. “Takeda’s global presence, their pipeline that includes complementary products to Feraheme and their strength in the marketing and commercialization of therapeutics across many specialties where iron deficiency anemia is present makes them the ideal partner for Feraheme.”

Under the deal struck April 1, Takeda receives an exclusive license to Feraheme for all therapeutic applications in five regions: Europe, Canada, Turkey, the Commonwealth of Independent States and Asia Pacific countries—including Japan, China and Taiwan.

For this consideration, AMAG receives a $60 million upfront payment and is eligible to receive a sum as high as $220 million in development and commercial milestones. In addition, AMAG will receive tiered, double–digit royalties based on net sales of Feraheme in the licensed territories.

The terms of the deal call for AMAG to execute and fund the global clinical development of Feraheme in all potential therapeutic indications. AMAG will also be initially responsible for the filing of regulatory applications for Feraheme in Europe and Canada, with Takeda responsible for the regulatory filings in all other regions covered by the agreement. Takeda will eventually hold all marketing authorizations in the licensed territories.

Finally, Takeda will be responsible for commercializing Feraheme in all regions included in the licensed territories.

“This partnership provides an exciting opportunity to combine AMAG’s unique development capabilities with Takeda’s global commercialization capabilities,” says Alan MacKenzie, executive vice president of international operations and CEO of Takeda Pharmaceuticals International Inc.

“Takeda is poised to maximize Feraheme’s entry into the selected countries following approval.”

From a governance standpoint, the companies will establish two joint committees to oversee the relationship, says David A. Arkowitz, executive vice president, chief financial officer and chief business officer of AMAG.

“The Joint Steering Committee, consisting of equal representation from each company, is responsible for overall coordination and oversight of the activities covered by the agreement,” he explains. “Also, a Joint Development Committee, also consisting of equal representation from both companies, will coordinate all elements of the development and approval of Feraheme in the territories covered by the agreement.”

In terms of AMAG’s $60 million upfront payment, the company is working with auditors to determine exactly how to represent and characterize it in the company’s profit and loss statements, Arkowitz says, but he doesn’t expect it to show up in the first-quarter profit and loss; rather, in some way after that quarter.

With a Japanese partner, why was Japan excluded from the terms of this deal? Arkowitz says that Japan and a few other territories will be part of future discussions with Takeda, but adds, “Takeda’s interest in Feraheme is in part based on the fit with their late-stage pipeline. Given the early stage of development of Feraheme as it relates to Japan we have not prioritized—and Takeda is not prioritizing—Japan in the same way as the EU and the other territories that are covered by this agreement. So this is something that’s not included in the agreement and we haven’t reached a final decision yet as it relates to Japanese rights.”

“The two dominant areas are the U.S. and the EU,” notes Pereira, though he says AMAG is enrolling patients for studies in countries outside of the United States and the EU. “Our emphasis at this point in time is to get the EU done … we have language about the cost sharing for those, but we haven’t released details yet.”

Currently, Feraheme is approved with the U.S. Food and Drug Administration for the treatment of iron deficiency anemia (IDA) in adult patients with chronic kidney disease, and AMAG plans to submit a marketing authorization application to the European Medicines Agency for Feraheme for the treatment of IDA in adult patients with chronic kidney disease in Europe in mid-2010. Additionally, AMAG plans to initiate a broad global registration program for Feraheme for the treatment of IDA regardless of the underlying cause in mid-2010.

“In the EU alone, more than a million people have chronic kidney disease and iron deficiency anemia. Outside of chronic kidney disease, an additional 4 million in the EU are estimated to have iron deficiency anemia,” Pereira says. “With a strong presence in gastroenterology and primary care, Takeda is poised to maximize Feraheme’s entry into the licensed territories following approval.”

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IBBL

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Luxembourg’s leading public research and academic centers developed the IBBL to accelerate medical research in personalized medicine with a focus on developing new diagnostic biomarkers.

Personalized medicine, according to Dominic Allen, COO of the IBBL, is a paradigm shift in the treatment of disease. Personalized medicine takes into account factors unique to each individual under treatment—factors such as metabolomics and genetic composition, Allen adds.

“Medicine traditionally has been the application of treatments as defined by the disease,” Allen explains. “In personalized medicine, we make treatment not only a function of the disease, but of the individual.”

To further this new practice, IBBL partners with companies such as Life Technologies to provide expertise in technologies to analyze the banked tissues samples. The IBBL was founded, according to Allen, to both become a state-of-the-art biobank, as well as support research with carefully selected partners.

“We supply samples and data of various natures, which provides an infrastructure from which our research partners, such as Life Technologies, can conduct its work in their areas of expertise, such as sequencing,” Allen adds.

IBBL currently conducts sequencing analysis, and distributes a wide variety of the high-quality biopspecimen samples while ensuring the strictest confidentiality and protection of donors’ data. IBBL has the technology and expertise to provide valuable genetic and molecular information in addition to medical records and environmental factors related to the donor.

From Life Technologies, the IBBL will adopt company’s Applied Biosystems SOLiD System, which Life Technologies calls “the most accurate next-generation sequencing platform available today,” to sequence the IBBL’s extensive variety of samples.

This work could result in greater understanding of the genetic basis for many diseases, and could have application in various areas such as disease-based research and in the future, sequencing for clinical diagnoses.

“We’re pleased to become the sequencing technology partner to IBBL,” said Mark Stevenson, president and chief operating officer of Life Technologies, in a prepared statement. “Our SOLiD system is the perfect technology to be used for sequencing IBBL’s well-characterized samples, and we look forward to working with them to advance their goal of being a leader in the advancement of personalized medicine.”

“By partnering with Life Technologies, IBBL is gaining access to cutting-edge sequencing technology, an important step to building an advanced technology infrastructure and a successful biomedical research industry in Luxembourg,” says Dr. Jean-Claude Schmit, president of IBBL. “Working hand-in-hand with one of the leading companies in the field and contributing to new developments will allow IBBL to have early access to constantly evolving technologies and to offer the highest quality genetic data to our research collaborators.”

IBBL’s Allen describes the pact as a partnership agreement, and not as a contract per se.

“This is a partnership agreement on a combination of things, not as a ‘deliverables’ contact,” Allen comments. “We have a commitment to working together.”

He says part of that combination includes upgrades to equipment and publishing of research papers over time.

Life Technologies representatives did not comment on the relationship by press time.

Co-founded in 2008 by Luxembourg’s three public research centers and the university, and developed in partnership with TGen, IBBL is part of a major strategic effort to help the country develop cutting-edge skills and expertise in molecular medicine. Its new facility opened on Feb. 25, ddn

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Autism story hits close to home for ddn reporter

BY STEPHEN ALBAJNY-JENI

THE DISCOVERIES of technologies and advances involved in the deals our editors and reporters write about each month sometimes hit very close to home. Such was the case this month for Lori Lesko, who brings us a story about Melior Discovery’s partnership with the Rett Syndrome Research Trust to screen drug candidates in an in vitro model of Rett Syndrome, the most physically disabling of the autism spectrum disorders (see page 33).

Autism is a condition with which Lori has become intimately familiar. In 1999, Lori married Mike Lesko, who is also a journalist in Northeast Ohio. Inspired by their work on a series of stories about local couples that adopted children from other countries, Lori and Mike decided to venture abroad—a move that would eventually lead to a Bureachest orphanage to meet the child they would rename and raise as Michael in their Bed ford, Ohio home.

But soon after their arrival, the Leskos realized that Michael was not the same active, mischievous child they saw in the video.

“The video had no sound, so we didn’t know that at 22 months old, he had not spoken—not even baby talk,” Lori says. “We knew something was wrong because he would race around the room and not look at us, but we put that down to fright. He understood Romanian, so we figured he would learn English. He learned English within six months at home with us, but still did not make the proper sustained eye contact that would allow him to even mimic baby sounds, much less speak.”

Michael would later be diagnosed with Pervasive Development Disorder (PDD), a developmental condition on the autism spectrum, and the Leskos eventually learned from an international adoption expert that infants who live in orphanages often have similar challenges because the lack of interaction leaves them too young to develop normally. The brain synapses to remain dormant.

“This means a child does not talk (no one to mimic), the child cannot stand to be touched; the child will slap, pinch, etc., if you get too close to his face, the child will rock back and forth or stare at his hands, refusing to make eye contact,” Lori explains. “Michael’s doctors and teachers have been supportive, but his doctors reiterate that Michael’s trust and primary diagnostic is organic brain damage—not from being dropped or abused, but from the failure of relating to a human as a baby. To make a long story short, autism is the diagnosis used because he exhibits signs of autism. However, we don’t think in any way of knowing, whether his condition is genetic.”

As Lori continues to search for those answers, she set out this month to discover more about autism and the Rett Syndrome Trust is doing for autism patients.

“I now see more opportunities in terms of clinical trials and different therapies to keep autism focused,” Lesko says. “But by the time the FDA approves something, Michael will already be in his teens. The problem is, the general public, and parents of autistic children, seem to want to try all kinds of things, like diet and drugs. But nothing really attacks the brain in a way that would ‘cure’ autism.”

Not yet, anyway. Let’s hope the best chapter is yet to come in young Michael’s compelling story.

The Patent Reform Act of 2010: A substitute S. 515

The Patent Reform Act of 2010 in the form of an amendment to S. 33. The amendment would address a number of improvements to the patent laws, such as provisions to update and improve the patent marking statute. By eliminating the arcane and subjective rules associated with the current first-to-invent system, the amendment will make it easier and less costly to obtain patent protection in the United States, which will stimulate investment in new technologies. Moreover, while all inventors will continue to benefit from a one-year grace period in which to file a U.S. patent application after publicly disclosing their inventions, the incentive of the first-inventor-to-file system to file applications promptly will benefit in obtaining patents in our major trading partners. Inventors who delay filing their U.S. applications (on the erroneous assumption that they will be able to obtain a U.S. patent by proving that they were first to make the invention) run the risk of being second-to-file in the rest of the world where patents are awarded to the first inventor to file.

The amendment will strengthen patents granted in the United States by allowing the public to participate in the patent granting process and by strengthening the administrative procedures in the U.S. Patent and Trademark Office (USPTO) for reviewing patents after grant. The bill will expand the opportunity for the public to submit information to patent examiners working on individual patent applications, together with comments and evidence to support their views.

The amendment will provide a robust, post-grant review that must be requested within nine months after patent grant and, if initiated, be completed within one year. Patents could be challenged for invalidity. While both the initial post-grant review and the revised inter partes re-examination proceedings will contribute to ensuring that only valid patents will survive, both procedures also contain safeguards to prevent harassment of patent owners. Both procedures will be handled by a panel of administrative law judges. Importantly, patent owners who promptly file meet the patent grant will be assured that the court will not automatically stay its consideration of the patent owner’s motion for a preliminary injunction on the basis that a petition requesting a post-grant review has been filed or that such a proceeding is pending in another forum.

The amendment would address a number of litigation reforms. For example, it would initially rescind provisions of the National Academy of Sciences (NAS) and others, some quite controversial, urged by various special interest groups. The amendment addresses the recommendation of the NAS to modify or remove the subjective elements of patent infringement litigation that depend on the assessment of a party’s state of mind and increase the cost and decrease the predictability of such litigation. Under the bill, “failure to disclose the best mode shall not be a basis on which any claim of a patent may be canceled or held invalid or otherwise unenforceable.”

Another of the subjective elements of patent infringement litigation that unnecessarily increases the costs for both obtaining patents and litigating them is the doctrine of inequity in conduct—whether an inventor or patent attorney intentionally misused the USPTO in prosecuting the original patent. While the amendment does not go as far as modifying or removing the doctrine as recommended by the NAS, it does provide a remedial avenue for patent owners to bring to the attention of the office information which might affect the scope of their patents. The bill allows patent owners to file a “supplemental consideration” action to consider any information believed to be relevant to the patent. Any patent surviving such reexamination will not be held unenforceable on the basis that such information had not been considered or was incorrect in the initial examination process.

Importantly, supplemental reexamination would avoid patent owners and others based on violations of criminal or antitrust laws nor would it allow those responsible for any misconduct in proceedings before the office to avoid disciplinary sanctions.

The amendment maintains the compromise reached in the Senate Judiciary Committee that fully responds to allegations of inconsistency and unfairness in awards of reasonable royalty patent damages. It rejects the proposals calculated to reduce inventors’ recoveries by narrow claims inventions through the use of definitional devices by limiting the claimed invention for damages purposes to “its inventive contribution, its patentable features” or “the patent’s specific contribution over the prior art.” Instead, the bill sets forth a “gatekeeper” approach which ensures that courts or juries consider only those damages contentions that are cognizable at law and supported by substantial evidence.

The third subjective element in patent litigation addressed by the NAS is willful infringement, under which a court may increase damages up to three times if the court or jury determines that the accused infringer willfully infringed a patent. In response to a growing number of patent infringement cases filed by patentees in perceived pro-plaintiff venues with little or no connection to the parties in the case or the locations of their operations, witnesses or documents, proposals were made to essentially restrict patent suits to the jurisdiction where the infringer had its principal operation. This draconian rule would have denied manufacturing patentees the opportunity of bringing suit against infringers in the district where the patentee was located and had its witnesses and evidence.

Stephen AlbaJny-Jeni is a patent attorney at Frost Brown Todd LLC, serving up chat at PatentBaristas.com. Further analysis of the amendment to S. 515 can be found on that Web site. Write AlbaJny-Jeni with comments or questions at Stephen@patentbaristas.com.
COMMENTARY: What drug discoverers should know about interferon and its future

A deeper understanding of interferons’ varied functions within the immune system may lead to discovery of more effective therapies

BY DR. SIDNEY PESTKA

Ver the last several decades, interferon (IFN)-based therapeutics have come to represent hope, survival and quality-of-life improvements for countless individuals suffering from multiple sclerosis, cancer or severe infectious diseases. Yet, continuing research on the many functions of IFNs leads us to believe that we have only scratched the surface of these molecules’ therapeutic potentials.

While numerous laboratories continue to build on the clinical success of the alpha interferons Roferon-A and Intron-A (IFN-α2a and IFN-α2b, respectively), the first FDA-approved biotherapeutics for treating hairy cell leukemia, and subsequently, hepatitis B and C infections. For example, the effectiveness of IFN-α2 in combating HCV has been dramatically improved through combination with the nucleoside analogs for approved indications, researchers and clinicians are actively examining new clinical indications where IFNs may improve patient outcomes. In particular, oncology is a rapidly expanding area quickly from the circulation, frequent IFN administration generally is required to foster any resolution of solid tumors. Yet frequent, high-dose administration of IFNs often triggers serious side effects such as depression, flu-like symptoms, and hematological sequelae. With the development of pegylated IFNs yielding increased half-life and more stable IFN levels in the circulation, patients can receive lower and less frequent IFN doses typically accompanied by less severe side effects than those of the standard IFNs. Still, although pegylated IFNs have greatly improved the clinical outcomes of patients with viral infections such as hepatitis C, the utility of these modified IFNs in treating patients with solid tumors has been more elusive.

In an attempt to improve the understanding of the structure-function differences between the different IFN-α subtypes, and in some cases, to design improved IFN-α therapeutics, several laboratories and companies have pursued limited or aggressive IFN mutagenesis or hybrid approaches. In addition to giving rise to one further approved IFN-α (Infergen), a single, pegylated IFN adds the excitement of chronic hepatitis C, these research programs as a whole have shaped our understanding of contact regions between IFN and the type 1 IFN receptor, and have delineated select amino acid residues within the IFN-α proteins that are crucial to high affinity binding or highly effective signal transduction.

As already mentioned, the key to realizing IFNs’ full potentials as therapeutic agents lies in understanding their diverse mechanisms of action, particularly the immunological pathways that are activated, inhibited, modulated, or otherwise engaged by these molecules. While extensive basic research into IFNs opened the door for their use in the treatment of several diseases, recent development research and (un)suspected gains have led more heavily toward expanding the clinical applications of the very few approved IFN molecular entities rather than pursuing additional members of the family with regard to their clinical utilities. The impact of this shift has had both positive and negative consequences. On one hand, several seminal papers have engendered heightened interest in the potential for IFN-α to prevent and better treat disease. Through the drive of this community and the willingness to take on projects with substantial risk, several IFN-α molecules become central to improving quality of life of millions of patients worldwide. Nearly 1,000 clinical trials currently mention IFN alpha, beta and gamma, with more than 600 clinical trials mentioning IFN-α2a alone. With the 2008 worldwide market for IFN-based therapeutics estimated at approximately $8 billion, it is remarkable and surprising how much remains unclear regarding the many functions and effects of these proteins. Fortunately, we are in the midst of an exciting resurgence of interest in the IFN field. In order to expedite the discovery of new and effective IFN therapeutics and that induce or inhibit IFN expression and/or function, we must strive toward a deeper understanding of each IFN’s signaling pathways in various cell types, each IFN’s functional impact on immune and cancer cells and each IFN’s unique physiological sequelae in patients.

The key to realizing IFNs’ full potentials as therapeutic agents lies in understanding their diverse mechanisms of action, particularly the immunological pathways that are activated, inhibited, modulated, or otherwise engaged by these molecules.

By Dr. Sidney Pestka

Dr. Sidney Pestka is known as the “father of interferon” for his early, groundbreaking work leading up to the beginning of the industry, including the first recombinant interferons for the treatment of cancers, leukemias, viral diseases such as hepatitis B and C and multiple sclerosis. Pestka is currently chairman and professor of the Department of Molecular Genetics and Immunology at UMDNJ Robert Wood Johnson Medical, and the founder and chief scientific officer at PBL InterferonSource.
**INSTRUMENTS & INFORMATICS**

**Deal is cut and dried**

Luminex acquires automation firm BSD Robotics, expanding expertise in field of dry sample handling

**By Lloyd Dunlap**

**AUSTIN, Texas—** Luminex Corp. has acquired BSD Robotics in a deal the company says will provide it with new technologies in automation and robotics in the field of dry sample handling. The firms did not disclose the acquisition price.

Privately held BSD Robotics, headquartered in Brisbane, Australia, operates in several markets, including newborn screening, forensics and human identity molecular diagnostics. It is among the world’s leaders in the design, manufacture and supply of high-technology laboratory instruments (and the associated software) used in the preparation, prior to processing, of biosamples dried on media. Established in 1991, BSD develops and markets both fully automated and semi-automated systems, such as BSD LaserCutter & BSD600V, now being released, which focuses on all new forms of bio-sampling devices, including plastic framed sample cards such as BioDisks, and buccal cell collection devices such as VibraSwabs and SwabGrips.

Luminex develops, manufactures and markets biological testing technologies, with a broad range of life-science applications based on its proprietary xMAP technology, which enables companies and laboratories to perform biosassays more quickly and cost-effectively than with other systems without sacrificing accuracy, says Russ Bradley, the company’s vice president.

**A good fit for sequencing**

CLC bio partners with Ion Torrent to expand high-throughput sequencing support

**By Jeffrey Bouley**

**CAMBRIDGE, Mass.**— CLC bio recently announced a partnership with Ion Torrent, a new sequencing company started by Dr. Jonathan Rothberg, the founder of 454 Life Sciences, through its regular sales and distribution channel. According to the companies, the agreement is an initial step that allows Pall and SOTAX deliver automation-certified solutions for pharmaceutical testing systems

**PORT WASHINGTON, N.Y.—** Pall Corp., a developer of filtration, separation and purification systems, announced in March a long-term, joint marketing agreement with the SOTAX Group, a Switzerland-based developer of test instruments and software for tablet testing by the pharmaceutical industry. At the start of the agreement, all new SOTAX AT 70smart Dissolution systems and SOTAX CTS Content Uniformity test systems will include the Pall Acordis PSF syringe filters. Filter refills will be available directly from Pall Life Sciences through its regular sales and distribution channel. According to the companies, the agreements an initial step that allows the companies to begin delivering complete certification solutions that save time and testing costs for quality control laboratories.

**Shimadzu, Cerno Bioscience partner to improve data calibration**

**COLUMBIA, Md.—** Shimadzu Scientific Instruments has partnered with Cerno Bioscience to offer Shimadzu’s LCMS quadrupole systems along with Cerno’s MassWorks software in an agreement aimed at helping users to improve data calibration for more accurate mass determination. In conjunction with Shimadzu’s LCMSsolution software, the package uses Cerno’s patented MSIntegrity calibration technology to improve mass accuracy by up to 100 times, while achieving spectral accuracy on unit mass resolution mass spectrometers. According to the companies, the package enables researchers to perform accurate compound identification through elemental composition prediction, a capability usually only available on more expensive high-resolution systems.

**Transcending clinical trial hurdles**

**Acquisition of TranSenda adds clinical trial management software to BioClinica’s portfolio**

**By David Ruffton**

**NEWTOWN, Pa.—** BioClinica, a Pennsylvania-based clinical trial management services company, has signed an agreement to purchase TranSenda International, a Bellevue, Wash.-based developer of clinical trial management software.

The terms of the deal call for TranSenda shareholders to receive a total of $77,060 shares of BioClinica stock as compensation for the purchase. For 2010, BioClinica expects TranSenda to contribute approximately $1 million in service revenue and an operating loss of $500,000. Additional financial details will be provided when BioClinica releases its first quarter 2010 results and full-year 2010 guidance, which will include TranSenda’s contribution.

BioClinica will continue to maintain an office in the Seattle area. Key employees were retained and several positions were eliminated as a result of this acquisition. TranSenda President Robert Webber will assume a vice president post with BioClinica.

“The acquisition of TranSenda not only enhances our portfolio of clinical trial technology, it also provides us intellectual property with thought leaders and domain experts in trial planning and management,” says Mark Weinstein, CEO of BioClinica. “We welcome Bob Webber and his team to BioClinica.”

Weinstein says the TranSenda acquisition represents an important advance in the execution of BioClinica’s integrated eClinical solutions strategy.

**BioClinica continued on page 16**
Bring the power, performance, speed, and long reads of the GS FLX Titanium chemistry to your benchtop with the newest addition to the Roche genome sequencing portfolio – the GS Junior Sequencing System.

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For complete information on the GS Junior System and all of the Roche sequencing solutions, visit www.454.com or contact your local Roche representative today.

Figure 1: Example Read Length Distribution of 100,000 reads from *E. coli* K-12 (genome size approximately 4.5 Mb), from a single GS Junior System run.

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Symyx partners with Simulations Plus

BY LLOYD DUNLAP
SUNNYVALE, Calif.—A new modeling tool will explore the world’s largest database to improve the predictive modeling of metabolites and accelerate exploration of viable drug candidates. Under the agreement, Simulations Plus Inc. will use information from the Symyx Metabolite database to develop a new system for in silico predictive modeling of metabolic properties, enabling R&D organizations to improve compound design, drive down experiment costs and reduce late product failures.

The improved model will be incorporated into a new Symyx Metabolite module, which is expected to be offered as part of the Simulations Plus ADMET Predictor software suite later this year. Simulations Plus supports advanced drug design modeling of properties associated with absorption, distribution, metabolism, elimination and toxicity of chemical substances in humans. Modules include physico-chemical and biopharmaceutical properties, toxicity, Enedlin metabolism, simulation and a customizable ADMET risk filter.

“One of our explicit aims is the development of a predictive mathematical model that will be capable of identifying specific sites of metabolism,” says Walt Woltsz, chairman & CEO of Simulations Plus. He calls such site-specific information the key. “Charge distribution is important to figure out where the enzyme—with UGT and CYP being the two most common—is acting. Quantum calculations can take a day, ADMET Predictor can handle almost 300 descriptors and 60 predicted properties per molecule and still reach an impressive performance of just under 250,000 molecules per hour for typical inputs using a laptop computer.”

In general, Woltsz adds, the program’s speed depends on input complexity. Woltsz notes that the model is a work in progress with a useful version expected by year’s end. “A quality model requires quality data,” notes Carmen Nitsche, vice president of Symyx’s content business unit. “We are very pleased to be working with Simulations Plus on a tool that will improve the reliability of metabolic biotransformation modeling for ADMET researchers.”

The Symyx Metabolite database includes about 13,000 parent compounds and 95,000 known biotransformations. The company’s professional scientists abstracts collect relevant in vivo and in vitro data in the correct format, Nitsche notes, so that none of the information is “siloed.”

Symyx garners xenobiotic transformations and metabolic schemes from published sources and conference proceedings, as well as non-proprietorial metabolism studies from new drug applications published by the U.S. Food and Drug Administration. Metabolite is unique, Nitsche states, because it enables researchers to discover complex metabolic pathways across articles in the literature, helping researchers better and system degrade, pathways of known compounds in humans and animals.

Commenting on her company’s recent merger with Accelrys, Carmen Nitsche says she believes the broad portfolio that results from the merger and the new agreement with Simulations Plus will add value for customers. Symyx products also include a market-leading electronic laboratory notebook (ELN) and decision support software solution. In another value-added convergence, a component for Accelrys’ Pipeline Pilot is distributed with the ADMET Predictor program together with installation instructions.

“Commenting on her company’s recent merger with Accelrys, Carmen Nitsche says she believes the broad portfolio that results from the merger and the new agreement with Simulations Plus will add value for customers.”

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CLC CONTINUED FROM PAGE 14

“CLC bio is one of the leading developers of high-throughput sequence data analysis software, so we are pleased for the opportunity to partner with them,” says CEO and chairman of Ion Torrent, Thomas Knudsen.

As part of the promotional efforts of its technology, Ion Torrent will award two Ion PGM sequencers this spring through a grant program designed to help make DNA sequencing accessible to all scientists.

CLC bio is supporting this grant effort by supplying a lifetime license for CLC Genomics Workbench to both of the two winning grantees.

The Ion PGM Sequencer Grant Program is designed to foster the development of new applications for DNA sequencing that leverage the instrument’s speed, scalability and low cost.

“ Ion Torrent technology enables scientists to do experiments they never thought were possible, and that freedom will foster innovation and drive breakthroughs in research,” Rothberg says. “We look forward to working with scientists around the world to create applications that will transform healthcare.”

Lasse Göröltz, head of global public relations and marketing for CLC bio, says the partnership came about in part because CLC bio is also partnering with Raindance Technologies, with which Rothberg also serves in “an instrumental capacity.”

“So he and his team already knew us and what we stand for,” Göröltz explains. “As Ion Torrent has a core strategy of focusing on the platform itself and creating an ecosystem of partners around their technology, it made even more sense to partner so they didn’t have to write software for analyses like the second-generation sequencing companies have done. Last but not least, we’re already supporting all the other major sequencing technologies out there—Sanger, Illumina, SOLID, 454, Helicos, and PacBio when they launch later this year—which makes it relatively straightforward to pick us as we’re perceived as the leading software developer in high-throughput sequence analysis—a perception we like and don’t think is undeserved.”

Göröltz says the participation in the grant program with Ion Torrent came about as a natural extension of the partnership.

“We had no pressure from Ion Torrent to participate,” he says. “We simply think it’s a great idea to supporting creative and innovative research, and we like to support efforts like these as we also have done in the past. And of course we hope the winners will see the benefit of having industry-leading software that plays nicely with their new sequencer. That will surely enable a lot of non-programmers to get a successful endeavor when wanting to analyze all the data their new PGM instrument can churn out.”

CLC bio will continue to evolve with Ion Torrent’s platform, Göröltz says, which he notes will help ensure users always have full support and integration.

“It’s not unthinkable that after Ion Torrent’s launch we will be part of some interesting sequencing projects—perhaps even with some customization involved, as we have done with other platforms in the past,” he says.

Looking at short-term and long-term synergies with the CLC bio’s strategic goals as they mix with Ion Torrent’s, he adds: “In the short term, no Ion Torrent customers will be left out in the cold so to speak, not having a viable solution to analyze their data, and we even enable researchers to mix the datasets from the different instruments to perform hybrid assemblies. On longer term, partnering with Ion Torrent fits absolutely perfectly within our overall strategy of providing a one-stop solution for high-throughput sequence data analysis that plays nicely together with all the different platforms.”

For more information, visit www.DrugDiscoveryNews.com
Lab training for French-speaking Africans

WASHINGTON, D.C.—The American Society for Microbiology (ASM) recently completed the first French language course for laboratory diagnostic testing of tuberculosis, developed using funding from the President’s Emergency Plan for AIDS Relief (PEPFAR), and organized by the ASM’s International Laboratory Capacity Building Program (LabCap). The course focused on Mycobacterium tuberculosis, and was held Feb. 22 to March 5 in Abidjan, Côte d’Ivoire.

This course is part of an effort led by ASM, through its LabCap Program, under the governance of the LabCap Committee housed within the ASM International Board, and supported by the Centers for Disease Control and Prevention’s (CDC) International Laboratory Branch of the Global AIDS Program, which aims to create training opportunities for French- and Portuguese-speaking lab professionals in Africa and other resource-limited settings. To date, courses developed for the African Center for Integrated Laboratory Training are presented in English, and thus not accessible to most people from PEPFAR-supported countries such as Angola, Cameroon, Democratic Republic of Congo, Haiti and Mozambique.

LabCap is now working with the CDC to develop another French-language course, focusing on acid-fast bacilli microscopy, and has just released a new textbook to assist in the roll-out in Dakar, Senegal, in August.

New edition of ASM Press biotechnology text

WASHINGTON, D.C.—ASM noted on March 2 that Molecular Biotechnology: Principles and Applications of Recombinant DNA is now in its fourth edition, bringing it “thoroughly up-to-date with the latest findings and the latest industrial, agricultural, pharmaceutical and biomedical applications.”

“It has been estimated that worldwide there are currently several thousand biotechnology companies employing tens of thousands of scientists. When the exciting science being done at universities, government labs, and research institutes around the world is factored in, the rate of change and of discovery in the biological sciences is astounding,” says Bernard Glick of the University of Waterloo, who co-authored the book with Jack Pasternak, also of the University of Waterloo, and Cheryl Patten of the University of New Brunswick.

Virology text focuses on families

WASHINGTON, D.C.—Earlier this year, ASM Press published a new virology textbook that educates the reader by focusing on the families. Based on the author’s experiences teaching virology for more than 35 years, Virology: Molecular Biology and Pathogenesis is said to enable readers to develop a deep understanding of fundamental virology by emphasizing principles and discussing viruses in the context of virus families.

“This book is meant to be used as a textbook for a comprehensive virology course aimed at advanced undergraduate and graduate students. It was conceived and organized to express my avid belief that the best way to teach virology is to discuss viruses in the context of virus families,” says author Leonard Notkin of the University of Massachusetts, Amherst.

Small organisms in the big city

Pharma and surfing mecca
San Diego plays host to this year’s ASM meeting

BY JEFFREY BOULEY

SAN DIEGO—While the American Society for Microbiology (ASM) may be based in Washington, D.C., where so much legislative and regulatory activity takes place that directly impacts the pharma and biotech world, the organization is taking its educational and professional networking to one of the nation’s hotbeds of pharma and biotech research and development: San Diego. That effort would be in the form of the 110th General Meeting of the American Society for Microbiology, being held May 23-27 at the San Diego Convention Center.

In addition to the nearly five days of scientific programming, there are also pre-meeting workshops on Saturday and before the beginning of the meeting on Sunday, May 23. In all, the scientific program will feature nearly 300 individual colloquia, symposia, roundtable discussions, award lectures and poster sessions. Things kick off Sunday evening, at 5 p.m., with the presentation of scientific topics of general interest to ASM members, followed by the ASM Lecture at 6 p.m.

This year, the meeting will offer such sessions as “Nanotechnology and Infectious Diseases” and “Microbes in Extinction Events,” in an attempt to bring together diverse aspects of microbiology that are relevant to today’s evolving world. According to Jim Sliwa, manager of media relations for ASM, a special session focusing on the microbiome may be of particular interest to attendees, “as it seems to be an emerging topic of interest in microbiology these days.”

Overall, the meeting will do an excellent job of covering the recent developments, advances and controversies in all areas of microbiology including clinical microbiology and epidemiology, pathogenesis and host defense, general and applied microbiology, microbial physiology, genetics and molecular microbiology, environmental microbiology and evolution, parasitology and virology, according to Dr. Jeffery F. Miller and Dr. Margaret McFall-Ngai, the chair and vice chair of the General Meeting Program Committee, respectively.

Miller and McFall-Ngai also note that they and ASM feel honored to have three renowned microbiologists set to be present for the opening general session on Sunday.

“Dr. Stephen Quake of Stanford University will present the ASM Lecture, and Dr. Antje Boetius from the Max Planck Institute for Marine Microbiology and Dr. Yoshihiro Kawaoka from the University of Wisconsin School of Veterinary Medicine will focus on technology and revolutions in microbiology,” they note.

“This year’s meeting will highlight recent advances in microbial cell biology, genetics and physiology, environ-
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BY JEFFREY BOULEY
SAN DIEGO—The Orange County and Los Angeles area often comes to mind when people think of Southern California, yet San Diego is a place of distinction as well, as the second-largest city in California and the ninth-largest in the nation—and Forbes magazine listed it as the fifth-wealthiest city in the United States. And, of course, as the readers of ddn well know, the city and its surrounding area is a hotbed of pharmaceutical and biotech activity.

Let’s run down a few of the heavy hitters there—no, not folks like Amylin, Amados Pharmaceuticals, Exelixis Inc., Ligand Pharmaceuticals, or any of the many other companies based there or with major operations there. We’re going to talk about some of the biggest entertainment destinations.

SAN DIEGO ZOO
One of the premier zoos in the United States, this facility is a sanctuary for thousands of animals and rare plants, including the famous giant panda exhibit. Other exhibits include a 7.5-acre multispecies habitat featuring elephants, condors, jaguars and more that is designed specifically for off-road travel to take riders close to wildlife, or the Flightline, a zip-line attraction that allows visitors to walk through a submerged tube while sharks swim around them; the Wild Arctic and Penguin Encounter exhibits; a California tide pool exhibit; a freshwater aquarium and the World of the Sea aquarium; Wonders of the River; and the Sesame Street Bay of Play.

LEGOLAND CALIFORNIA
This park reflects just how varied and thematic the LEGO toys themselves have become over the decades, with rides, shows and attractions in areas with such themes as heroes and adventurers, a lost kingdom, pirates, knights and more.

BEACH LIFE
It is Southern California, so you might want to hit the beaches.

Plenty to do, from beasts to blocks to beaches

If you didn’t get enough animals at the San Diego Zoo itself, or weren’t satisfied that the enclosures were realistic enough, try a visit to the zoo’s 23-acre Wild Animal Park, a separate location featuring huge open enclosures that allow herds of African and Asian animals to roam and interact with each other. Visitors can get up close to these wild and endangered animals thanks to the Journey into Africa tour, which emulates safari tours in Africa but with vehicles that run on biodiesel for a more eco-friendly vibe.

Newer and more adventurous ways to explore the park include tooling around on a two-wheeled electric personal transporter that is designed specifically for off-road travel to take riders close to wildlife, or the Flightline, a zip-line attraction that allows people to soar over the park.

SEAWORLD
Certainly, Shamu the killer whale is the most famous denizen of this aquatic animal park, but there is also a the Shark Encounter, which allows visitors to walk through a submerged tube while sharks swim around them; the Wild Arctic and Penguin Encounter exhibits; a California tide pool exhibit; a freshwater aquarium and the World of the Sea aquarium; Wonders of the River; and the Sesame Street Bay of Play. ddn

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DOWNTOWN DYNAMICS

BY JEFFREY BOLEY

SAN DIEGO—Downtown San Diego is unlike many metropolitan downtown areas, framed by inland mountains and one of the most beautiful natural harbors around. The historic Gaslamp Quarter, for example, features Victorian-era buildings and numerous fine restaurants, as well as 35 pubs and nightclubs and 100 retail shops—in addition to theaters, art galleries, offices and residential/work lofts. Dining in this neighborhood is considered by many to be a global culinary journey, with such cuisines as Afghan, Brazilian, Chinese, Indian, Italian, Mexican, Persian, Spanish, Thai and more.

For the largest downtown neighborhood, visit East Village, encompassing 130 blocks and revitalized from a once-blighted warehouse district. Now it is home to luxury hotels and restaurants, rooftop bars, cafés, boutique shops, galleries and live music venues scattered throughout the neighborhood.

For a more specific ethnic flavor, there’s always the Little Italy neighborhood, which was once home to the city’s tuna fishing industry. Attractions include patio cafes, restaurants, pubs, art galleries, shops, hotels and Amici Park. Cuisines feature dishes from both Southern and Northern Italy.

We’ll conclude with one more neighborhood, Horton Plaza, which is notable or being named after its main resident attraction, also called Horton Plaza, a multi-level outdoor shopping and entertainment center. Since 1985, Horton Plaza has offered 130 specialty shops, restaurants, a movie theatre, and performing arts theatre. The center was created to resemble a European marketplace and function like an amusement park with colorful pathways, bridges and staggered levels.

FILLING YOUR BELLY

A premier list to help you please your palate

From the Web site sandiegoeater.com comes this list of top destinations for “overall dining experience.” You can also visit the site to find out the top locations for service, food, ambiance, value and bar/wine selection.

Best Restaurants: Overall Dining Experience

• Basì Ristorante (Italian cuisine, located in Old Town)
• Bistro at Mister A’s (American cuisine, located downtown)
• Blue Sea Bar and Grill (American cuisine, located in Point Loma & Ocean Beach)
• Caffè Bella Italia (Italian cuisine, located in Pacific/Mission Beach)
• Delicias (California cuisine, located in North County Inland)
• Downstairs (Steak restaurant located downtown and in La Jolla)
• George’s California Modern (California cuisine, located in La Jolla)
• Mille Fleurs (California cuisine, located in North County Inland)
• Primavera Ristorante (Italian cuisine, located in Coronado)

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**DIAGNOSTICS**

**BRIEFS**

**Access Genetics to market Caliper’s MDx system**

**HOPKINTON, Mass.**—Caliper Life Sciences Inc. announced in April a non-exclusive original equipment manufacturer agreement with Access Genetics to market Caliper’s LabChip GX microfluidic system for molecular diagnostic applications. The LabChip GX system provides laboratories that offer DNA diagnostic testing a platform for automating numerous molecular tests on a common instrument system. As part of the agreement, Access Genetics will incorporate Web-based software, materials and protocols developed specifically for use with the LabChip GX and market the combined platform’s benefits to a wide community of clinicians, pathologists and physicians. Financial details of the agreement were not released.

"For 10 years we have awaited an instrument platform that realizes the potential of miniaturized DNA-based diagnostics,” says Dr. Ron McGiennen, founder, president and medical director of Access Genetics. "The LabChip GX platform is a versatile and economical solution for clinical molecular applications."

**Biomedical Diagnostics to distribute Asuragen’s oncology products in France**

**AUSTIN, Texas**—Asuragen Inc. in April appointed Biomedical Diagnostics SA, a medical diagnostic company in Europe, as its exclusive distributor of Signature Oncology Products in France. The portfolio comprises multiplex assays for the detection of mutations in solid and hematologic malignancies, including a research assay for KRAS and BRAF mutations, the Lux CE marked IVD assay to detect fusion transcripts in total RNA from whole blood or bone marrow to aid in the clinical diagnosis of translational positive leukemias and an assay for the simultaneous detection of the most common NPM1 Mutations. All of these assays utilize multiplex RT-PCR followed by multiplex detection on the Luminex 100 IS or 200 System. Financial terms of the deal were not disclosed.

**Enzo Biochem in supply agreement with Cancer Genetics**

**NEW YORK**—Enzo Biochem Inc. announced in April a supply and distribution agreement between Enzo Life Sciences and privately owned Cancer Genetics Inc., a producer of nucleic acid products used in genomic research. The agreement covers Enzo’s proprietary fluorescent dye labels for increasing signal intensity in labeling nucleic acids. The non-exclusive agreement enables Enzo Life Sciences to incorporate its proprietary labeling to increase specificity for CGI’s nucleic acid material that it purchases and supplies to the research market. According to Enzo, the integration gives the CQI probe greater visual sensitivity and the potential for improved clinical value and patient outcomes. Financial details were not released.

**Diagnostics**

**Signed, sealed, delivered**

PerkinElmer acquires diagnostic genetic testing firm Signature Genomics

**BY AMY SWINDEMAN**

**WALTHAM, Mass.**—Viewing its diagnostic services business—which has continued to produce double-digit yearly growth in recent years—as a viable unit for expansion, PerkinElmer Inc. has acquired Signature Genomic Laboratories LLC, a diagnostic genetic testing company based in Spokane, Wash.

The deal, announced in mid-April, is intended to strengthen PerkinElmer’s existing genetic service testing business, which is heavily concentrated on prenatal and neonatal screening systems as well as clinical diagnostic systems, instruments and accessories and software.

According to Jim Corbett, president of ViaCord, a cord blood banking and clinical research arm of PerkinElmer’s genetic screening and research arm of PerkinElmer in North America, the acquisition also aims to expand the company’s position in early disease detection—specifically in the molecular diagnostics market—and provide the company with additional strengths in cancer diagnostics.

"We look forward to expanding our molecular diagnostics capabilities and services, and expect the acquisition to enable us to take our technologies to the rest of the world, potentially offering a product model," Corbett says. "We also see cancer diagnostics as an adjacent market for us to move into. The first line of products we develop will be for hematological cancers. We have targeted nine different types to which we will apply microarray technology. We’re also looking at solid tumor opportunities."

Founded in 2003, Signature Genomics is well known as the first laboratory to provide microarray-based cytogenetic diagnostics, but had humble beginnings. The company opened its doors with just three employees, and after starting to offer testing in March 2004, made a profit by August of that year. After an infusion of cash from stakeholders Ampersand Ventures and Jven Capital, Signature was able to grow to more than 100 employees and has made more than 6,000 diagnoses after processing 40,000-plus cases since the

**Partnership is air for the lungs**

Source BioScience inks deal with AstraZeneca to provide genetic testing service for lung cancer

**BY DAVID HUTTON**

**NOTTINGHAM, U.K.**—Source BioScience has announced that it will provide drugmaker AstraZeneca with a companion diagnostic testing service for lung cancer patients in the United Kingdom.

This service will be funded by AstraZeneca and will allow clinicians in the National Health Service to identify whether lung cancer sufferers have activating mutations in their tumors making them sensitive to tyrosine kinase inhibitor therapies. Knowledge of the genetic status of the cancer will help clinicians determine the most appropriate therapy regime for lung cancer patients. Financial terms of the agreement have not been publicized.

According to Dr. Nick Ash, managing director at Source BioScience, the focus of the agreement is the timely provision of a sophisticated molecular diagnostic test that will assist in determining whether lung cancer patients should or should not be offered treatment with Iressa (gefitinib).

Under the agreement, Ash says Source BioScience will arrange transport of patient samples to AstraZeneca for analysis.

**Best served at room temperature: Just add water**

GenVault provides GenTegra DNA to support cardiac genetic testing at Berkeley HeartLab

**BY KIMBERLEY SIKH**

**CARLSBAD, Calif.**—GenVault Corp. recently announced that Berkeley HeartLab, a subsidiary of Celera Corp., has adopted GenTegra DNA to preserve and store diagnostic samples for genetic testing related to the management of cardiovascular disease.

As new clinically important diagnostic genetic markers are introduced, such as KIF6 (a gene variant associated with non-fatal myocardial infarction among certain carrier populations), accessing stored DNA eliminates the need to collect a new sample and facilitates the expedited return of potentially critical medical information to the physician, the companies say.

Rene Nunez, director of marketing for GenVault, points out that Berkeley HeartLab’s adoption of GenTegra DNA in handling and processing of samples will reap numerous benefits for the high-volume facility.

“They intend to use the GenTegra DNA to preserve and store diagnostic samples for genetic testing focused on cardiovascular disease,” Nunez says. GenVault provides GenTegra DNA to support cardiac genetic testing at Berkeley HeartLab.
Companies Seeq infectious disease answers

Novartis to market Smiths Detection’s Bio-Seeq instrument and technology for infectious disease diagnostics

BY LLOYD DUNLAP

LONDON—Smiths Detection, whose diagnostics unit develops ruggedized instruments designed for easy operation by specialists in veterinary and clinical procedures, has signed a collaboration and license agreement with Novartis Diagnostics under which Novartis is granted exclusive rights to market Smiths Detection’s Bio-Seeq instrument and the associated LATE PCR DNA analysis technology in the area of infectious disease diagnostics.

Under the agreement, Smiths Detection will leverage its expertise in instrument development and point-of-care diagnostic devices to further enhance the Bio-Seeq platform and sample preparation consumables and to develop a range of diagnostic tests. Novartis Diagnostics will be responsible for clinical trials, regulatory affairs, sales and marketing. Financial terms of the agreement were not disclosed, but payments will be linked to product development and commercial milestones.

According to Smiths Detection, the Bio-Seeq platform enables rapid, flexible and highly precise detection of bacterial and viral pathogens and is designed for users with little or no experience of biological testing. The tests use LATE PCR, a variation on conventional PCR that was originally developed by Brandeis University for which Smiths Detection holds an exclusive license. A LATE PCR reaction produces a large excess of single stranded DNA that is analyzed at the end point of the reaction. The technique allows highly multiplexed assays to be developed.

The Bio-Seeq instrument is a simple-to-use, sample-in/answer-out desktop instrument capable of running five LATE PCR tests simultaneously. The planned enhancements include increasing the number of simultaneous tests to 20 with the addition of slave units. A disposable sample preparation unit, which is used across a wide range of tests, and a reagent pack, which is particular to the test being run, round out the system.

“We are evaluating multiple advances to both the technology and the platform,” says Daniel Parera, Novartis’ head of development. “In addition, the platform will be tailored to address the needs of a hospital or laboratory, rather than a field-based setting. Although both require very fast time-to-results, clinical diagnostic user interfaces, reports and workflow will be optimized based on detailed human factor studies and clinical needs.”

Peter Maag, president of Novartis Diagnostics, notes that “Smiths Detection and Novartis Diagnostics have a passion for preventing the spread of infectious diseases through collaborations such as this. Our aim is to address a significant unmet need for accurate and accurate early treatment and to guide physician decision making and improve outcomes.”

“[THE] TECHNOLOGY HAS A RANGE of potential diagnostic applications in the area of infectious diseases. Our aim is to address a significant unmet need for adequate and accurate early treatment by developing tests to guide physician decision making and improve outcomes.”

—Daniel Parera, Novartis’ head of development

Smiths Detection provides advanced security solutions in civil and military markets worldwide, developing and manufacturing government-regulated technology products that identify explosives, chemical and biological agents, weapons and contraband. It is part of Smiths Group, a global leader in applying advanced technologies for markets in threat and contraband detection, energy, medical devices, communications and engineered components. The Smiths Group employs around 22,000 people in more than 50 countries.

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Optimizing breast cancer therapy strategies

Health Discovery and Smart Personalized Medicine to develop technology for lab tests aimed at personalized breast cancer therapy

BY LLOYD DUNLAP
SAVANNAH, Ga.—Health Discovery Corp. (HDC) and Smart Personalized Medicine LLC (SPM) have entered into development and related licensing agreements with Quest Diagnostics Inc., a leading provider of diagnostic testing, information and services. Under the agreements, Quest Diagnostics will develop new laboratory tests for aiding in the selection of breast cancer therapies based on technology provided by HDC and SPM.

SPM was formed by Dr. Richard E. Caruso, who founded and is now chairman of the board of directors at the billion-dollar health company, Integra LifeSciences Holdings Corp., to focus on and enable the development of a new method of accomplishing detailed breast cancer patient diagnosis and personalized individual treatment. In 2006, Caruso was named the Ernst & Young National Entrepreneur of the Year for the United States following his founding of Integra LifeSciences.

Health Discovery owns an equity position in Smart Personalized Medicine. In February 2009, Health Discovery announced that it had licensed rights to develop a new urine-based test for clinically significant prostate cancer to Quest.

Under the terms of the agreements, HDC and SPM will receive upfront licensing payments, development fees and royalties on a per-test basis from Quest Diagnostics.

“Richard Caruso has been a long-time supporter of Health Discovery and served on our board,” notes HDC chairman and CEO Dr. Stephen D. Barnhill. “We saw an opportunity to deploy our patented Support Vector Machine technologies in the area of breast cancer. Specifically, we wanted to identify the optimal therapeutic strategies for women diagnosed with breast cancer. We were confident that we had the right partner in Richard Caruso and view the opportunity to work with him as the most expeditious way to apply our technology in this area.”

Health Discovery is a molecular diagnostics company that uses advanced mathematical techniques such as Support Vector Machine (SVM) technologies to analyze large amounts of data to uncover patterns that might otherwise be undetectable. It operates primarily in the emerging field of personalized medicine where such tools are critical to scientific discovery. Its primary business consists of licensing its intellectual property and developing its own product line of biomarker-based diagnostic tests that include human genes and genetic variations, as well as gene, protein and metabolic expression differences and image analysis in digital pathology and radiology.

“Our patented-protected technology allows for this kind of discovery,” Dr. Barnhill says. “It’s been proven in previous test developments, such as our prostate cancer test, that have applied SVMs and RFE-SVMs. We expect to identify a molecular signature in patients that will allow doctors to identify the correct therapy.”

RFE-SVM is used to find discriminate relationships within clinical datasets and within gene expression datasets created from microarrays of tumor versus normal tissues. Using the technique, HDC scientists have been able to access specific genetic information that other advanced bioinformatics techniques missed. For example, RFE-SVMs are able to filter irrelevant, tissue-specific genes from those related to malignancy. RFE-SVM also identifies gene expression patterns related to severity of the disease. The data analysis technique provides physicians with patient-specific information and is an enhanced decision-making tool for pharmacogenic and toxicological profiling of the patient.

HDC scientists note that RFE-SVM’s analytic methods are effective for finding genes implicated in several cancers.

“In the case of genomic biomarkers,” Barnhill notes, “they will sometimes be identifiable in tissue, blood and urine, which is what we discovered with our four-gene biomarker for clinically significant prostate cancer.”

In 2009, it is reported that there were approximately 275,000 people in the U.S. and 1.2 million people worldwide diagnosed with breast cancer.

“Increasing demand for targeted therapies to improve treatment success and reduce costs is generating greater demand for companion diagnostics to accompany those therapies,” he says. “The market for cancer diagnostics during 2010 is predicted to be in the region of $5.4 billion, with an increasing requirement for molecular diagnostics based on genetic analysis. If we are able to provide better diagnostic information for clinicians, this will help ensure that treatment pathways are managed more effectively, positively impacting the clinical outcome and cost effectiveness of therapy.”

Each sample will undergo full pathology review prior to genetic testing, which will enable the tumor status to be determined, ensure that only tumor tissue is analyzed and guarantee the highest quality of diagnostic analysis and reporting.

Ash points out that the ultimate success of the agreement will be judged on turnaround times and percentage of successfully evaluated samples.

Other U.K. diagnostic companies, including Lab21 Ltd. and DxS Ltd., now owned by Qiagen NV, are also providing tests for potential Iressa patients.

Source BioScience also last month released new tests to allow researchers to test for mutations in the NRAS and BRAF genes, conditions which are linked to certain cancers.

The company says it has developed the new pyrosequencing assays using its in-house expertise, with the tests being designed to be suitable for use with FFPE material. Mutations of NRAS and BRAF are found in those affected by a number of different cancer types, including melanoma, colorectal cancer and myeloid leukemia.

According to Source BioScience, the release of the NRAS test represents the first assay of its kind to be made available in the U.K.

The company is also providing tests for a number of critical samples.

SOURCE CONTINUED FROM PAGE 22

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— Dr. Nick Ash, managing director, Source BioScience

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The company added that the launch of the new assays will allow for the analysis of cellular pathways, as well as assisting clinicians in developing new cancer treatments and categorizing patients for medical trials.
GENVAULT CONTINUED FROM PAGE 22

risk and disease,” Nunez explains. The technology, he says, is an innovation in stabilizing biosamples.

Specifically, Nunez continues, “GenTegra DNA is comprised of inorganic matrix with built-in oxidative protection and antimicrobial activity for dry, room temperature transport and biobanking of purified DNA. It is provided in ready-to-use aliquots, and purified DNA dried within GenTegra DNA is simply and fully resolubilized with water for direct downstream molecular analysis.”

Not only can samples be stored at room temperature and resolubilized simply with water, cost savings in sample handling can add up quickly in high-volume facilities such as Berkeley HeartLab, Nunez points out. The technology can also be considered a tool in promoting “green” laboratory practices, he says.

“Their use of GenTegra enables them to transport and store nucleic acids efficiently and cost effectively at ambient temperature and in the dry state while ensuring the integrity of their nucleic acid samples, Nunez adds. “Their adoption of the GenTegra technology is a step in the right direction towards sustainable biosample handling procedures is welcome: “At Berkeley HeartLab, the further integration of genetic tests into the standard panels of cardiovascular diagnostics requires efficient, high-quality DNA handling and management. GenVault’s GenTegra DNA provides a robust infrastructure for supporting our genetic testing business,” Amos says.

GenVault provides risk-free biosample workflow, transport and storage solutions for genomic medicine, discovery and identification. It counts among its clients pharmaceutical companies, medical centers, academic institutions and law enforcement agencies. As a scalable, reliable and environmentally friendly alternative to traditional freezers and nucleic acid purification systems, the company’s dry-state platform enables the extraction, preservation, recovery and distribution of biosamples at ambient temperature. According to Nunez, other customers who utilize GenTegra DNA include Centre Hospital De L’Universite Montreal, Dow Agrosciences, Genome Quebec Canada, Life Technologies, Scripps Genomic Medicine and University Health Network.

Berkeley HeartLab is a CLIA- and CAP-certified testing laboratory that maintains a comprehensive list of assays that utilize state-of-the-art genetic testing. Its laboratory processes approximately 1,000 samples per day and performs more than 200,000 tests per month. The facility offers services to predict cardiovascular disease risk and improve patient management.

Celera is a healthcare business focusing on the integration of genetic testing into routine clinical care through a combination of products and services incorporating proprietary discoveries. Celera also commercializes many molecular diagnostic products through Abbott and has licensed other relevant diagnostic technologies developed to provide personalized disease management in cancer.

More info: www.sbsonline.org/vc
**SIGNATURE**

**CONTINUED FROM PAGE 22**

Signature Genomics’ broad and butter comes from its proprietary SignatureChip technology, which is an oligonucleotide-based microarray specifically designed, developed and validated by cytogeneticists exclusively for clinical applications. According to Signature Genomics, the 133,000 oligonucleotides on the SignatureChip cover every region known to be involved in cytogenetic abnormalities, including over 200 syndromes, the pericentromeric regions, and subtelomeres, with a maximum probe spacing of one probe every 35 kb throughout the genome and one probe every 10 kb in clinical regions.

Signature’s microarray diagnostic technology is available for both prenatal and postnatal identification of DNA alterations associated with genetic disease. More recently, Signature launched a suite of services for the diagnosis of patients with leukemia.

Companies who do business in this fast-growing segment have come to recognize the face of Signature Genomics, Dr. Lisa G. Shaffer, as a leader in the field of genetic testing. A co-founder of Signature Genomics along with colleague Dr. Bassem A. Bejjani, Shaffer was named a national finalist for the Ernst & Young Entrepreneur Of The Year 2009 Award in Health Sciences.

“Lisa Shaffer is very well-known in the industry, as hers was the first service lab to take the microarray technology traditionally used in research and bring it to clinical use for the identification of developmental disorders in children,” Corbett says. “She has taken that expertise and now has an offering in the prenatal space, but is looking to enter the oncology space as well. She has an experienced staff that is well regarded in the research community.”

Signature Genomics did not respond to an interview request by press time. Shaffer said in a statement, “As a global leader in genetic screening technologies and services, PerkinElmer clearly has the resources and worldwide presence to enable our combined testing services to reach more patients and families. We believe that this move will not only benefit patient populations around the world, but help us continue our success in genetic diagnostic innovation.”

Financial terms of the acquisition, which is expected to close in May and is subject to customary closing conditions, were not disclosed. Corbett says Signature Genomics will retain its Spokane facility, which houses 120 employees who will become part of PerkinElmer’s genomics group.

Sara Gratton

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**ExonHit eyes growth in MDx market with RedPath acquisition**

PARIS—ExonHit Therapeutics SA, a developer of therapeutics and diagnostics tests, announced April 26 that it entered into a binding agreement for the acquisition of RedPath Integrated Pathology Inc., a privately held molecular diagnostics company focused on cancer, for $12 million in cash and $10 million in stock.

RedPath will become part of ExonHit’s U.S. operations in Gaithersburg, Md. Starting in 2012, RedPath’s current shareholders may receive subsequent additional payments of up to $9.5 million dependent on the achievement of specific sales targets. The transaction, which is subject to approval by ExonHit’s shareholders, is expected to close by mid-July.

Headquartered in Pittsburgh, Pa., RedPath has a DNA-based technology platform, PathFinderTG, which provides diagnostic information that can lead to a more personalized patient clinical management decision. According to RedPath, the analytical tool improves the diagnosis of difficult cases in which cancerous or precancerous conditions are not identified by a conventional pathology examination.

ExonHit says the addition of RedPath’s DNA platform to its RNA-based platform is a “synergistic addition” that directly links the significant role DNA mutations play in altering the regulation of alternative splicing. It is currently estimated that more than 10 percent of all described human gene mutations directly impact splicing.

The combined approach will allow for the possibility of more accurate diagnostic tests with a strengthened P position, says Dr. Luc Maurel, president of ExonHit’s management board.

“This transaction will strengthen our presence in the U.S., which represents 55 percent of the multi-billion dollar molecular diagnostics market. RedPath provides a strong strategic and business fit with ExonHit,” Maurel says.
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Making siRNA research a SNALP

Tekmira to use stable nucleic acid-lipid particle technology to deliver Pfizer’s siRNA molecules

BY DAVID HUTTON

VANCOUVER, B.C.—Tekmira Pharmaceuticals Corp. recently announced the initiation of a research collaboration with Pfizer Inc. According to Mark Murray, president and CEO of Tekmira, the collaboration focuses on evaluating Tekmira’s stable nucleic acid-lipid particle (SNALP) technology to deliver small interfering RNA (siRNA) molecules provided by Pfizer.

RNAi therapeutics have the potential to treat a broad number of human diseases by “silencing” disease-causing genes. The discoverers of RNAi, a gene silencing mechanism used by all cells, were awarded the 2006 Nobel Prize for Physiology or Medicine.

RNAi therapeutics, such as “siRNAs,” require delivery technology to be effective systematically. Lipid nanoparticles (LNPs) are one of the most widely used siRNA delivery approaches for systemic administration. Tekmira says its SNALP (stable nucleic acid-lipid particles) technology is the leading class of LNP’s being used in clinical development. SNALP technology encapsulates siRNAs with high efficiency in uniform lipid nanoparticles that are effective in delivering RNAi therapeutics to disease sites in numerous preclinical models. SNALP-based products have been reviewed by multiple FDA divisions for use in clinical trials. SNALP formulations comprise several lipid components that can be adjusted to suit the specific application.

“Tekmira will be responsible for preparing the SNALP formulations, and Pfizer will evaluate the formulations in preclinical models,” Murray says.

The companies have not revealed financial details of the collaboration. Specific diseases or therapeutic areas also have not been disclosed.

“We are pleased to be working with Pfizer, one of the world’s leading pharmaceutical companies and an organization that has made a commitment to the development of nucleic acid therapeutics,” adds Murray. “The collaboration combines Tekmira’s expertise in the delivery of RNAi therapeutics with Pfizer’s research excellence in nucleic acid therapeutics.”

Murray points out that Tekmira continues to collaborate with pharmaceutical and biotechnology companies, thereby broadening Tekmira’s presence in the nucleic acid therapeutics field.

Building a Better Mousetrap

Affymetrix and Jackson Laboratory announce the official commercial launch of groundbreaking mouse diversity genotyping array

BY JEFFREY BOULEY

SANTA CLARA, Calif.—Affymetrix Inc. and Bar Harbor, Maine-based Jackson Laboratory recently kicked off the full commercial launch of the Affymetrix Mouse Diversity Genotyping Array, with Affymetrix actually selling the array and Jackson Lab making it available as part of the JAX Mouse Diversity Genotyping Array Service.

Both the California company and the New England nonprofit biomedical research institution tout the product as “the first high-density genotyping array that enables researchers to study the complexity of the mouse genome and the diversity among mouse strains.” The significance of this, they note, lies in part because mice and humans share genomes of similar size, content and organization.
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Emory University School of Medicine and Zirus team up to create new class of antiviral drugs

BY KIMBERLEY SIRK

ATLANTA—The Emory Institute for Drug Discovery and Zirus Inc., a biotechnology company based in Buford, Ga., have inked a collaboration agreement that is expected to result in novel compounds to treat infectious viral disease. One of the goals of the partnership is to develop a broad-spectrum antiviral, much the same as the broad-spectrum antibiotics that currently exist to treat bacterial infections.

Zirus uses a proprietary method for identifying genes and gene products in host cells that, when blocked, can prevent viruses from multiplying. Over the past several years, either alone or in collaboration with partners, including the Centers for Disease Control and Prevention (CDC), Zirus has identified, licensed and filed patents on more than 1,000 such targets.

Infection is caused by viruses that are able to introduce genetic material into a host cell. Viral replication involves multiple steps, each of which provides a potential point for antiviral intervention. Zirus has identified a number of drugs currently approved for indications other than infectious disease that appear to also be effective in blocking targets that Zirus has identified. These drugs, having already successfully obtained a nod from the FDA, have the potential to reach the market quickly to address significant unmet medical needs for infectious diseases.

The Emory team working with Zirus has successfully brought a number of important drugs to market and is generally regarded as one of the top chemistry groups in the world.

Viral infections can be caused by a variety of viruses including influenza, H1N1, HIV, HCV, RSV, common cold viruses, bioterror threats and broad-spectrum antivirals, much the same as the broad-spectrum antibiotics that currently exist to treat bacterial infections. One of the goals of the partnership is to develop a broad-spectrum antiviral, much the same as the broad-spectrum antibiotics that currently exist to treat bacterial infections.

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Since viruses invade human cells and hijack proteins to reproduce, the goal of the combined forces of the two partners is to shut down the pathway for the virus to reproduce. “We seek to develop drugs that will be少年 magical spell to turn the virus into stone,” says David Perryman, president and CEO of Zirus. “We find and validate those host proteins, while Emory will then develop drugs to hit the key molecule in this equation.”

“Great viruses, viruses have shown that they can outsmart vaccines and antiviral drugs such as protease inhibitors by mutating and developing resistance,” says Dr. William O’Brien, Zirus’ chief medical officer. “As a result, they are now more effective at vaccine for HIV. Each year we need a new vaccine for the seasonal flu, the effectiveness of vaccines for variations of swine flu and avian flu remain questionable, and the cocktail of drugs taken by AIDS patients to reproduce, the goal of the combined forces of the two partners is to shut down the pathway for the virus to reproduce. “We seek to develop drugs that will be少年 magical spell to turn the virus into stone,” says David Perryman, president and CEO of Zirus. “We find and validate those host proteins, while Emory will then develop drugs to hit the key molecule in this equation.”

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“Infectious disease needs a multi-pronged attack, and the Zirus host targets appear to represent the ‘third leg of the stool’ along with vaccines and traditional antivirals that attack the virus.”

—Dr. Dennis Liotta, head of the Emory Institute for Drug Discovery

Currently, according to Liotta, the six-month-old partnership involves three post-doctoral chemistry students, who are conducting computational analyses. When “hits” are identified, additional human resources will begin to work on addition development.

Both sides would share in the financial return on the results. Neither partner would share details of that part of the agreement.

The Emory team is led by Dr. Dennis Liotta, the Samuel Candler Dobbs Professor of Chemistry and head of the Emory Institute for Drug Discovery. Liotta has won numerous awards for his work, has served as a consultant to a number of major pharmaceutical companies and is the inventor of record for several clinically important antiviral drugs. Liotta is also a member of Emory University’s Scientific Advisory Board.

“While I have successfully worked for many years developing antiviral drugs, the Zirus approach to blocking host cell genes and gene products represents a new paradigm

Dicer is a critical enzyme involved in the RNAi gene silencing cascade and acts earlier in the pathway, processing double-stranded RNA into ‘message’ molecules that are then recognized by the cellular machinery and directed to the target genes.

Under the agreement, Dicer is a private biotechnology company with a proprietary platform of more than 1,000 human host targets essential for viral replication and is developing repurposed drugs and preclinical small-molecule antagonists. Its platform addresses all major antiviral markets, including pandemic/seasonal flu, HIV, cancer, cold viruses, bioterror threats and broad-spectrum antiviral drugs.

The Emory Institute for Drug Discovery was established in August 2009 at Emory University in Atlanta, with the dual mission of carrying out early-stage discovery and preclinical development of small-molecule therapeutics and training new generations of researchers in a multidisciplinary drug discovery environment.

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ISIS
CONTINUED FROM PAGE 1

Isis will be eligible to receive license fees and milestone payments totaling nearly $1.5 billion. In addition, Isis will receive up to double-digit royalties on sales from any product that is successfully commercialized.

Dr. Patrick Vallance, senior vice president and head of drug discovery at GSK, said in a statement released by the company that Isis’ antisense approach offers an exciting opportunity to target certain severe diseases in a way that has not previously been possible. Antisense therapies target the proteins involved in disease processes through the RNA that is involved in building these proteins. Isis’ discovery platform develops specific therapies that bind to messenger RNA (mRNA) and inhibit the production of disease-causing proteins.

“Isis Pharmaceuticals is a leader in antisense technology, and this new alliance will enhance our discovery platform in this promising research area,” Vallance stated. Dr. Stanley T. Crooke, Isis’ chairman and CEO, notes that the alliance differs from most traditional pharma collaborations in that it allows Isis to accept a bit more risk and retain

control of the discovery and early development of drugs while working with a high-quality partner who accepts a little less control to maximize the value of the drugs in late-stage development and commercialization.

“This alliance is exactly the type of deal we want to do,” Crooke says. “It has benefits for both companies. It gives us cash now and puts us in the driver’s seat in terms of drug discovery.

When we get to Phase II, we have a partner who is ready to license the drugs, so there is no delay in moving forward. It also means that our partner knows what it wants and can move with the speed and efficiency of a smaller company.” Although Isis has never worked directly with GSK before, Regulus Therapeutics Inc., a developer of microRNA therapeutics jointly owned by Isis and Alnylam, has had sev-

eral collaborations with the top pharma in recent years. Crooke points out that Isis’ antisense drug discovery platform is so efficient, the company discovers more drugs than it can develop by itself. Because of that, Isis licenses its drugs to partners prior to late-phase development and commercialization, eliminating the costs associated with a sales and marketing force. Isis then benefits from upfront license fees, milestone payments and royalties.

Some of Isis’ other many pharma partners include Genzyme, Bristol-Myers Squibb Co., Teva, OncoGenex and Novartis, Crooke notes. To date, Isis has generated more than $1.6 billion from the successful execution of its partnership strategy, and is the owner or exclusive licensee of more than 1,600 patents worldwide.

“If people are involved in RNA therapeutics, they generally end up dealing with us or one of our partners,” Crooke says. “We’re interested in moving more aggressively into some orphan diseases, as was GSK, so our common interests, Isis’ position at the center of the world of RNA therapeutics and GSK’s interest in seeking the type of deal we have done with other companies in the past led to productive conversations.”

TEKMIRA
CONTINUED FROM PAGE 2

the use of its SNALP delivery platform, with a goal to sign additional collaborative agreements in 2010.

“Tekmira’s SNALP technology is the leading class of lipid nanoparticles being used in clinical development for the delivery of RNAi therapeutics,” adds Murray. “SNALP technology efficiently encapsulates siRNAs in uniform lipid nanoparticles and enables the effective delivery of RNAi therapeutics to sites of disease. SNALP formulations are manufactured using a proprietary method that is robust, scalable and easily reproducible.”

Pooya Hemami, an analyst with Desjardins Securities, says the collaboration adds further validity and support to Tekmira’s SNALP technology, and that is what is driving investor interests.

This is Tekmira’s first formal research collaboration with Pfizer. Murray notes that Tekmira also is working with Alnylam Pharmaceuticals Inc. and Swiss drugmaker Roche Holding AG, both of which are developing drugs using the SNALP technology.

“So if other companies like Bristol-Myers Squibb and Pfizer, which have initial agreements with Tekmira, were to develop more comprehensive licensing agreements, it would be very positive to the extent of the depth of the potential revenue for the technology,” Hemami says.

One of the key issues raised with the SNALP technology is safety. In January, an early-stage trial for Tekmira’s own internal cholesterol drug candidate using the same technology showed that one of the two patients, treated at the highest dose level, experienced flu-like symptoms.

“My main concern really, and I think for a lot of analysts covering the company, is the safety of the technology. There were concerns with the first phase study of ApoII SNALP as there was a case of flu-like response,” Hemami notes. ddn

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MOUSETRAP

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and thus mouse-based studies are key elements in the quest to address human health issues. Reporting results of research on the array in August 2009 in Nature Methods, Affymetrix and Jackson Lab have shown evidence that the array is the first that can simultaneously assay 623,124 single nucleotide polymorphisms (SNPs), a hundredfold increase over other currently available arrays, and more than 900,000 invariant genomic regions in the mouse genome. They note that researchers can use it to genotype virtually any mouse, identify genetic changes involved in disease phenotypes and genetically monitor important laboratory mouse strains.

Through JAX Services the array is now offered to provide hybridization and computational analysis services to researchers worldwide, and the array service is being provided by the same microarray and computational analysis group that participated in the design, validation and analysis of the Mouse Diversity Genotyping Array. Jackson Lab has run more than 1,000 samples on this array so far.

“The natural variation between inbred mouse strains provides us with an essential tool to study complex diseases involving the interaction of multiple genes,” says Dr. Gary Churchill of the Center for Genome Dynamics at Jackson Lab, who developed the array along with Dr. Fernando Pardo-Manuel de Villena of the University of North Carolina. “This is a focal point of biomedical research and drug efficacy testing. Using Affymetrix technology, we have created a way for scientists around the world to analyze these arrays, and the only way to make it easily and widely available to many of them was for us to offer the JAX Mouse Diversity Genotyping Array Service,” he says.

“Affymetrix knew, and we realized, that there were a lot of people out there with interest in these arrays, and the only way to make it economically buy the arrays from Affymetrix. “Affymetrix knew, and we realized, that there were a lot of people out there with interest in these arrays, and the only way to make it easily and widely available to many of them was for us to offer the JAX Mouse Diversity Genotyping Array Service,” he says.

“The natural variation between inbred mouse strains provides us with an essential tool to study complex diseases involving the interaction of multiple genes. This is a focal point of biomedical research and drug efficacy testing. Using Affymetrix technology, we have created a way for scientists around the world to analyze these variations with much greater specificity and data reproducibility,” —Dr. Gary Churchill, Center for Genome Dynamics, Jackson Laboratory
**Research & Development**

**Resistance is futile**
NeurOp and Bristol-Myers Squibb to develop NeurOp’s NMDAR antagonists in treatment-resistant depression

**By Lloyd Dunlap**

ATLANTA—NeurOp Corp., recently announced a collaboration with Bristol-Myers Squibb Co. (BMS) focused on the development of NeurOp’s proprietary small molecules for use in the treatment of major depression and other central nervous system disorders. According to BMS spokesperson Jennifer From Maurer, “BMS was attracted to NeurOp’s molecular understanding of the target we are interested in, the NR2B receptor, and its collection of 400 compounds aimed at that target. We have established a working group with leadership from both companies to manage day-to-day activities. Both parties will work to identify new compounds active against the receptor, and then advance both new hits and early leads to a clinical candidate.”

Under the terms of the agreement, BMS has agreed to pay NeurOp an upfront fee of $1.5 million and to fund a two-year research collaboration. In addition, NeurOp is eligible to receive up to $73 million in potential milestone payments for the successful development of a compound in major depression and royalties on worldwide sales of commercialized compounds. The compound class to be developed is focused on generating new Alzheimer’s disease therapies focused on tau-targeted therapies for Alzheimer’s disease. The agreement contains potential royalties and milestone payments linked to successful clinical development and eventual worldwide marketing of target-specific compounds. Financial details were not released.

**ALLIES AGAINST AUTISM**

Rett Syndrome Research Trust, Melior Discovery to develop drug candidates for most disabling form of autism

**By Lori Lesko**

TRUMBULL, Conn.—Aimed ultimately at reversing the most physically disabling of the autism spectrum disorders, the Rett Syndrome Research Trust, a nonprofit, has joined forces with Exton, Pa.-based Melior Discovery Inc. to screen drug candidates and eventually develop effective therapies.

“This partnership is further illustration of Melior’s truly unique capabilities and competence in high-throughput, in vitro pharmacology,” says Andrew Reaume, president and CEO of Melior Discovery. In 2007, the journal Science published the work of chemist/researcher Adrian Melior of Cornerstone Pharmaceuticals.

**Cancer research turns a corner**

NCI taps Cornerstone Pharmaceuticals’ nanotechnology for evaluation of anti-cancer agents

**By David Hutton**

CRANBURY, N.J.—Cornerstone Pharmaceuticals says it has entered into an agreement with the National Cancer Institute (NCI) to collaborate on research involving the company’s proprietary nanotechnology. The agreement marks the first collaboration of this kind between Cornerstone and the NCI.

As part of the collaboration, Cornerstone will apply its novel lipid oil nanoemulsion to a class of anti-cancer agents developed by the NCI’s Center for Cancer Research Nanobiology Program. These agents, developed within the laboratory of renowned biologist Dr. Robert Blumenthal, can be turned into toxic compounds by targeted radiation and ultrasound. Cornerstone and NCI will evaluate the potential of these combined technologies in reducing tumors.

“From Cornerstone Pharmaceutical’s perspective, the U.S. National Cancer Institute, over a period of decades, has established the infrastructure to research how cells become cancerous, how to identify new drugs and treatments, models that can be used to predict what will happen in man and the ability to conduct clinical studies in accordance with U.S. FDA guidelines,” says Dr. Robert Shorr, CEO of Cornerstone Pharmaceuticals. “We believe that the researchers at the National Cancer Institute investigators with whom Cornerstone is collaborating are world class with some of the most innovative and exciting discoveries in cancer research emerging from their laboratories.”

Shorr notes that the specific development will contain a suite of lipid-based nanocarriers that will deliver a wide variety of cancer therapies, including small molecules, proteins, aptamers, and siRNA.

**Briefs**

AstraZeneca, Penn Medicine in Alzheimer’s disease therapy deal

PHILADELPHIA—The University of Pennsylvania’s Penn Medicine Center for Neurodegenerative Disease Research (CNDR) and AstraZeneca have signed a collaborative research agreement focused on generating new Alzheimer’s disease drug candidates for the clinical development pipeline. CNDR will provide access to drug compound screening assays and expertise with the protein tau. AstraZeneca scientists will supply basic drug discovery research and technologies. The agreement contains potential royalties and milestone payments linked to successful clinical development and eventual worldwide marketing of target-specific compounds. AstraZeneca has exclusive access to compound IP and study data for any commercial purposes. Specific financial details were not disclosed.

Sigma-Aldrich to sell Pfizer’s bioactive small-molecule compounds

ST. LOUIS—Sigma-Aldrich has entered into an agreement with Pfizer Inc. to sell approximately 100 Pfizer-developed small-molecule compounds to life science researchers for target characterization, assay development, screening and in vivo animal model applications. The Pfizer compounds, which include patented and approved drug molecules such as atorvastatin, sildenafil and celecoxib, will be made available to the research community while still on patent, in some cases for the first time. Sigma-Aldrich will sell the compounds as in-stock, pre-packaged items and, upon request, in bulk. According to the companies, the inclusion of these Pfizer compounds provides authentic material that will help advance researchers’ understanding of biological systems. Financial details were not released.

BioSeek and Ono begin multi-year drug discovery collaboration

SOUTH SAN FRANCISCO, Calif.—Asterand plc subsidiary BioSeek LLC and Japanese specialty pharma Ono Pharmaceutical Co. Ltd. have signed a three-year drug discovery collaboration agreement under which BioSeek will apply proprietary BioMAP platform on a specific drug target class designated by Ono, performing phenotypic screening and for hit identification, lead optimization and clinical candidate selection. According to the agreement’s terms, BioSeek will receive unspecified research funding and milestone payments upon achievement of a certain milestone by a drug candidate discovered under this collaboration. Ono will have worldwide rights to develop and sell all pharmaceutical products discovered through the collaboration.
Giving a lymph to patients

Moffitt Cancer Center receives NCI grant to create bioengineered “designer” lymph nodes with Scripps Florida

BY JEFFREY BOULEY
TAMPA, Fla. – Dr. James Mulé and his colleagues simply aren’t satisfied with the human immune system, and they aim to do something about it by creating lymph nodes. To aid in this effort, Moffitt Cancer Center, in collaboration with researchers at the Scripps Florida campus of The Scripps Research Institute, has been awarded a five-year, nearly $2 million grant from the National Cancer Institute to design lymph nodes for cancer immunotherapy.

“We believe we will no longer be held hostage by what Mother Nature has given us with respect to an immune system,” says Mulé, executive vice president of applied research at Moffitt. “We anticipate we will be able to create fully functioning, designer lymph nodes at will in the human body.”

The reason for the NCI’s interest is clear, Mulé notes, when you consider that a patient diagnosed with cancer has a dysfunctional immune system either because of the tumor or the treatment being used to eradicate the tumor. Designer lymph nodes could help rebuild a patient’s immune system to better fight disease and possibly even increase the potency of vaccines.

In this effort, Mulé is partnering with Dr. John Cleveland and Dr. Juliana Conkright, both at Scripps Florida in Jupiter, Fla., who will use high-throughput screening technologies to rapidly select the candidate genes to use in creating the human lymph nodes. A clinical trial related to melanoma is currently underway at Moffitt using one of the first candidate genes as a primitive lymph node. Twelve patients are enrolled. As Mulé describes it, the gene is introduced into a specialized immune cell that is a potent cell for presenting foreign antigens. These gene-modified antigen presenting cells are exposed to and/or incubated with tumor antigens to “load them up” and then simply injected under the skin. The injected cells then produce the protein from the inserted gene that will form the rudimentary lymph node structure within about seven days after injection.

A clinical trial related to melanoma is currently underway at Moffitt using one of the first candidate genes as a primitive lymph node. The gene is introduced into a specialized immune cell that is a potent cell for presenting foreign antigens. These gene-modified antigen presenting cells are exposed to and/or incubated with tumor antigens to “load them up” and then simply injected under the skin. The injected cells then produce the protein from the inserted gene that will form the rudimentary lymph node structure within about seven days after injection. "Upon completion of the initial Phase I trial—evaluating safety and immune response/rudimentary lymph node formation monitor-potency of vaccines," Mulé says. "In parallel, we, with our Scripps colleagues, will evaluate in the laboratory which of the remaining 47 or so genes should be employed to improve and further design the optimal lymph node. The results of that screen will determine the selection of the ‘next generation’ genes to move into the clinic."

As to whether such designer lymph nodes would augment existing lymph nodes or replace faulty or failed ones, Mulé says that both are part of his aims.

“Tumor rejection—the sky’s the limit,” he maintains. “They would be formed anywhere under the skin where the injected, gene-modified cells are located, and would function independently and specifically against whatever foreign antigen is decided upon, or more than one antigen for that matter.”

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NCI CONTINUED FROM PAGE 33

penedly or combined with other treatment modalities to more effectively treat tumors.

“Cornerstone sees an important aspect of the Nanobiology Program’s work is the ability to improve the penetration of tumors by drugs under development,” he says. “The Nanobiology Program is pioneering approaches to improve cancer drug delivery. In its collaboration with NCI, Cornerstone intends to facilitate new research that will leverage NCI resources to benefit public health. We consider it a privilege to be working shoulder to shoulder with scientists of their caliber.”

Cornerstone has been able to formulate multiple types of anti-cancer compounds in Emulsiphain, its novel lipid oil nanoemulsion. Shorr points out that Emulsiphain is designed to maximize drug concentration into tumor cells thereby enhancing the anti-cancer compound’s selectivity and specificity, leading to a potentially safer and more effective cancer treatment. This is of particular importance for those tumors that may be located in a site not accessible to surgical intervention. Examples include, but are not limited to, tumors of the brain, liver, pancreas and gallbladder.

Dr. Yossel Raviv, who works in the laboratory at the NCI, discovered that a class of agents may become toxic when delivered to cancer cells and activated by an external energy source.

“The NCI and Cornerstone are interested in developing a nanoemulsion platform for the delivery of hydrophobic radiation and ultrasound sensitive compounds to tumors in vivo,” Shorr adds. “This is an important step forward towards achieving the dream of safe and effective cancer therapy for the most difficult to treat cancer types.”

Shorr points out that many approved drugs as well as newer cancer selective agents in use or in development today are difficult to solubilize and rely on diffusion after intravenous or oral administration to reach tumor cells. Often drugs may be metabolized and cleared from the body prior to reaching their target and as cells are distal from a tumor’s vasculature, it is more difficult for a drug to reach a sufficient concentration to be useful.

While technology continues to be evaluated for increasing the concentration of drugs in a tumor mass, Shorr notes that some of these may actually inhibit the uptake of a drug into tumor cells. According to Shorr, there are advantages to Cornerstone’s cancer selective nanotechnology platform, Emulsiphain.

“In Cornerstone’s experience, some of the most useful anticancer agents are also the most difficult to dissolve and deliver to a tumor in a useful form,” he says. “The scientific literature demonstrates that the majority of the active ingredients in chemotherapies administered to treat tumors never make it to the target within the cancer cell. Cornerstone’s Emulsiphain drug delivery technology aims to overcome these challenges so that increasing the required effective dose doesn’t deliver treatment at the expense of risking a patient’s safety.”

An entire formulation science has arisen around the solubilization of poorly soluble drugs, Shorr adds. “How to make drugs become more specifically delivered to cancer cells and the site of their intended target has also been the subject of a tremendous worldwide research effort,” he notes. “There is the additional challenge of keeping drugs away from healthy cells and tissues that might otherwise be affected, to prevent unwanted side effects and morbidity. The challenge is to minimize the side effects of cancer chemotherapy and maximize drug tolerance and positive outcomes from cancer chemotherapy treatments.”

Numerous delivery approaches are being explored by other players, as well as Cornerstone. In addition, delivery approaches have complicated manufacturing schemes that are difficult to bring to commercial scale or result in products that have limited shelf-life and utility. Some delivery approaches also contribute to unwanted side effects.

“Many delivery approaches require chemical changes to be made to the drug in order to be compatible with the delivery technology,” Shorr says. “Others help to make drugs more soluble, but do not contribute to more specific delivery.”

For more information, visit www.DrugDiscoveryNews.com
Autism

Bird, demonstrating the reversal of Rett Syndrome in mature mouse models with late-stage disease. Only days away from death, these animals recovered normal function and became indistinguishable from healthy mice in a matter of weeks. This singular achievement has catapulted Rett into new realms of possibilities and positions Rett Syndrome to be the first curable childhood neurological disorder.

“The neurobiology of Rett Syndrome is proving to be complex and the treatment backward. These children lose speech, motor control and function, and many suffer from seizures, orthopedic and severe digestive problems, breathing and other autonomic impairments. Most live into adulthood and require total, around-the-clock care. The disorder is caused by alterations in a single gene, MECP2. The animal models that have been developed mimic the disorder well and provide an excellent system to test potential drug candidates. We look forward to our collaboration as we strive to identify compounds to ameliorate the devastating symptoms of Rett,” says Coenraads Coenraads, executive director of the Rett Syndrome Research Trust.

Unlike Asperger’s and other disorders on the spectrum, Rett Syndrome mostly occurs in females. MECP2 Duplication Syndrome has been recently identified, to date, mostly in males. Rett Syndrome “affects every system in the body, and its symptoms are severe and debilitating,” says Coenraads, mother to 13-year-old Chelsea, who was diagnosed with Rett Syndrome at age two.

The unexpected reversal of Rett Syndrome in animal trials “presents us with the urgent challenge of determining whether such results can be achieved in human sufferers of Rett Syndrome,” Coenraads says. “The neurobiology of Rett Syndrome is proving to be complex and the function of the MECP2 protein remains elusive. Basic scientists around the world remain focused on these issues. As this work progresses, there are clear approaches for intervention that must be pursued in parallel to understanding the function of MECP2, she said. RSRT has identified three such approaches: increasing levels of MECP2 protein; identifying new molecular targets; and taking a molecular target “independent” approach that focuses on functional improvement. The trust has embarked upon projects in each of these categories.

“Our collaboration with Melior focuses on the third approach—the screening of approved drugs and compounds to seek functional improvement in any of the debilitating symptoms,” Coenraads says. “This approach is a non-hypothesis driven approach, and in that respect, is complimentary to the first two approaches.

“The partnership came about after RSRT and Melior were introduced by renowned medicinal chemist Christopher Lipinski, who serves as an advisor to both organizations. Lipinski is best known for the Lipinski Rule of 5, which has become a critical filter for drug development. In his view, a compound was intended to emulate.

Melior has established a platform to allow for efficient and effective screening of existing drugs and compounds, and RSRT is eager to leverage this know-how for the identification of drugs/compounds that can alleviate symptoms, she says. Melior will also accept drugs/compounds from both academia and industry that have candidates for screening of existing drugs and compounds, and RSRT is eager to provide an excellent system to test potential drug candidates.

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The Melior strategy takes an opportunistic view of identifying therapeutic potential with existing drugs where the science has not yet advanced enough to show us how it is that a given compound would be beneficial in this complex disease, Coenraads says. Melior has established numerous examples of identifying otherwise unpredicted therapeutic potential in well-characterized compounds with well-characterized targets and mechanisms of action, she said. In the majority of these instances, this new therapeutic potential was an on-target effect driven by the molecular target for which the compound was intended to emulate.

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The ultimate goal of the partnership is to treat a broad spectrum of symptoms via drugs/compounds that were identified using Melior’s approach, she says. “I am hopeful that a cure for Rett Syndrome is in our future,” Coenraads says. “Unlike many disorders, Rett Syndrome has a gene, excellent animal models, the prospect of reversibility and a cadre of accomplished scientists. However, I recognize that developing a cure will entail an aggressive and unremitting effort both in terms of the science and amassing the financial resources that will be required to sustain that effort. We need new ways of informed and committed supporters to help us see the damage of Rett Syndrome reversed not in mice, but in humans.”

Monica Coenraads, executive director of the Rett Syndrome Research Trust, is pictured here with her main source of inspiration, her 13-year-old daughter Chelsea, who was diagnosed with Rett Syndrome at age two.
Pfizer to pay $142 million in damages for illegal marketing of Neurontin

NEW YORK—Following a month-long trial in U.S. District Court in Boston, a federal jury awarded plaintiffs Kaiser Foundation Health Plan Inc. and Kaiser Foundation Hospitals more than $142 million in damages, after finding that Pfizer Inc. fraudulently marketed Neurontin for unapproved uses, including bipolar disorder, neuropathic pain and migraine. Oakland, Calif.-based Kaiser claimed it was forced to pay $90 million more than it should have for Neurontin. The lawsuit also alleged that Pfizer misrepresented the drug’s efficacy. The jury, which deliberated for two days, found that Pfizer violated the federal Racketeer Influenced and Corrupt Organizations Act (RICO) and California’s Unfair Competition Law. Under RICO, the amount of actual damages found by the jury, $47.36 million, will be tripled. Chris Loder, a Pfizer spokesman, said the company was “disappointed” with the verdict and will file post-trial motions challenging the verdict and also appeal.

Caliper settles outstanding litigation with Shimadzu

HOPKINTON, Mass.—Caliper Life Sciences Inc. has entered into a settlement agreement with Shimadzu Corp. and its wholly owned subsidiary, Shimadzu Scientific Instruments Inc., resolving a lawsuit filed by Caliper in the U.S. District Court for the Eastern District of Texas that claimed Shimadzu’s MultiNA microchip-based electrophoresis system infringed several U.S. patents relating to Caliper’s microfluidic LabChip technology. Shimadzu denies infringement, but has discontinued sales of the MultiDNA system in the United States. The terms of the settlement were not disclosed.

Enzo Biochem may pursue damages against Life Technologies after court decision

NEW YORK—Enzo Biochem Inc. said last month that a decision by the Court of Appeals for the Federal Circuit reversing a district court’s summary judgment will enable the company to pursue a claim for substantial damages against Applera Corp., now Life Technologies Corp. The asserted patents cover technologies relating to compounds used in DNA sequencing systems to read the genetic code. The complaint against AppIera and its subsidiary Topigla Inc. charged patent infringement arising out of the misappropriation of Enzo’s proprietary and pioneering patented technologies related to DNA sequencing systems and other products, as well as providing others with unauthorized and prohibited access to the patented products and technologies.

Southern comfort

Genomics research takes hit in Minnesota

BY DAVID HUTTON

WASHINGTON, D.C.—President Barack Obama recently scored a political victory in the form of the recently approved healthcare bill. Whether the new legislation will have the pharmaceutical industry smiling or feeling blue remains to be seen.

It is known that the Patient Protection and Affordable Care Act will levy about $80 billion in various fees on the major pharmaceutical players over the next several years. It should also stoke sales by expanding drug insurance coverage. The bill also extends the period of market exclusivity for makers of biologic therapies, which are far more expensive to manufacture than traditional medications, to 12 years.

The legislation does not call for drug price controls or the importation of cheaper drugs from other countries, two possible scenarios that had been feared by many investors.

Absent from the legislation are provisions that would allow American consumers to buy reimported drugs from abroad and let the federal government negotiate drug prices, two controversial issues that the industry has said would devastate their balance sheets.

The approval of the legislation was applauded by Wall Street and could benefit the stocks of drug makers in the short term.

“I was unable to find anything in there that would cause me to have anxiety if I were a shareholder in a pharmaceutical company,” Ira Loss, a senior healthcare analyst at the research firm Washington Analysis, told The Wall Street Journal in the wake of the bill’s signing.

National Pharmaceutical Council President Dan Leonard said in a statement that the legislation offers the opportunity for meaningful change.

“Helping to inform healthcare decision making through comparative-effectiveness research ... has the potential for positively impacting patient health,” notes Leonard, whose group sponsors such research.

Meanwhile, MedTRACK, a leading database of private and public biomedical services, has stated that although the new legislation will have the pharmaceutical industry in the wake of the bill’s approval. Sarah Terry, president of Life Science Analytics, which produces MedTRACK, says that key reform measures in the bill will have an impact on society, private insurers, branded pharmaceuticals and generics.

“Measures such as the individual mandate, premium subsidies, Part D donut hole discounts/closure and the biosimilars approval pathway will have both positive and negative effects on these stakeholders,” Terry says.

BY JEFFREY BOGLEY

BAR HARBOR, Maine—Looking to create synergies with both its primary genetics research location in Maine and its much smaller campus in Sacramento, Calif., the Jackson Laboratory has been exploring the possibility of creating a new institute for personalized medicine in Florida. That was a plan that Jackson Lab announced in October 2009, and it’s a plan that Florida seems to be taking quite seriously, as state economic development officials there have been working on assembling a package of incentives that would bring Jackson Lab to their state.

The efforts of those officials have thus far led Florida’s House of Representatives and Senate to commit $310 million over three years, with $50 million of that earmarked for the fiscal year that starts July 1. That commitment was written into the compromise $69 billion budget that the state House and Senate were, at press time, expected to approve on April 30. The measure would then require the

Jackson Laboratory administrators insist that while the organization is very serious about possibly expanding to Florida with a new personalized medicine institute, it is also committed to retaining its base in Maine and expanding its Bar Harbor-based operations there.

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The court decision describes the stories of many patents on Myriad's breast cancer genes invalid, do you believe that genes should be patentable?

Yes, just like drugs/active chemicals/etc. are currently patented ........................................ 10.3%
Yes, but with a lesser number of years than traditional patents................................. 17.2%
Yes, but with mandated caps to fees for using patented genes................................... 0.0%
No ................................................................. 86.5%
Not sure/No opinion ........................................... 6.9%

READER POLL

We recently polled our readers on our Web site, www.drugdiscoverynews.com, about their opinions on the gene patent debate.

Following a New York federal court's decision rendering patents on Myriad's breast cancer genes invalid, do you believe that genes should be patentable?

Yes, just like drugs/active chemicals/etc.
Yes, but with a lesser number of years than traditional patents
Yes, but with mandated caps to fees for using patented genes
No
Not sure/No opinion
Institute. The other thing is that Jackson Laboratory Florida Jackson Labs that would be the want to establish a branch of to Florida,” Woychik says. “We necessary network of universities and medical schools for collabora- tion opportunities in the realm of personalized medicine.

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As branches of the Scripps, Torrey Pines, Burnham and Max Planck has already brought several top names inside its borders with a billion-dollar set of tax breaks, such as branches of the Scripps, Torrey Pines, Burnham and Max Planck research institutes, and it has the necessary network of universities and medical schools for collabora- tion opportunities in the realm of personalized medicine.

The thing is, we’re not moving to Florida,” Woychik says. “We want to establish a branch of Jackson Labs that would be the Jackson Laboratory Florida Institute. The other thing is that while we’ve only set up broad scientific parameters right now, one of our core aims is that what we would do in Florida would have to be different than what we do in Maine or California. We don’t want the new institute compet- ing with us but rather comple- menting us.”

What he seeks are not only dif- ferent types of activities, but also those that would create synergies capable of creating more work in Bar Harbor and Sacramento. In fact, along with the plans to possibly expand to Florida, Jackson Labs has plans to expand its Maine operation as well, and the Florida institute would not adversely impact those plans even if it does move forward, Woychik asserts.

“Maine is a great place to live, we have a great workforce, and the things that make Maine great allow us to attract talented people,” he says. “Jackson Lab would not have succeeded, would not be what it is today, and won’t be what it could in the future without those dedicated workers and the very strong support of the state of Maine. Our core oper- ations will remain here.”

It is estimated that the Florida institute would employ some 200 people within the first several years of operation. The existing locations of Jackson Lab employ more than five times that number. Since 2002, Jackson Lab has experienced sig- nificant expansion, with the total operating budget growing from nearly $304 million in 2002 to $470 million in the current fiscal year. In addition, the workforce has grown from 1,162 employees in 2002 to just over 1,300 employees today—roughly 90 of them in California. Also, during Woychik’s time as president and CEO, the organization has built some 118,000 square feet of new research and support space and has renovated 70,000 square feet of space. Over the next five to 10 years, Jackson Lab plans to add 200 more jobs to the Bar Harbor location, as well as expand from its current roster of 38 research groups to 45 such groups over the next five years or so.

Dr. Rick Woychik, president and CEO of Jackson Laboratory, calls the legislation for state funding “an important first step” in advancing the expansion project, but notes, “This is still very much a work in progress.”

“In the end, it will take not only the legislature coming up with $850 million, but also the county coming up with $130 million in matching funds,” he says. Also, he notes, Jackson Lab will be looking to phil- anthropic groups to come up with between $100 million and $150 mil- lion.

“If approved by the governor, the final budget will be an essential vote of confidence that will help us attract the institutional partnerships and the matching funds we would need for the project to proceed,” says Woychik, who also notes that approv- al by Jackson Labs’ board of trustees will also be required. In total, Woychik says that around $400 million will be needed in total to put up a building and recruit the best and brightest scientists.

“That’s our goal for a 10-year plan that will give us critical mass and allow us to bring around 25 investiga- tors to the location, and staff to support them,” he says.

Among the key factors driving Jackson Labs’ interest in establishing a personalized medicine institute in Florida is the need to be located in a state that already has other research institutes. Florida has already brought several top names inside its borders with a billion-dollar set of tax breaks, such as branches of the Scripps, Torrey Pines, Burnham and Max Planck research institutes, and it has the necessary network of universities and medical schools for collabora- tion opportunities in the realm of personalized medicine.
In the pharmaceutical industry, both branded and generics will experience some hardships of their own. Reform measures will force branded pharma to endure greater cost-containment pressures along with drug discounts.

Terry points out that more coverage and more prescribing doesn’t necessarily equate into better health in the long run,” she says. “The marketing activities of these companies will also suffer due to limitations the healthcare bill puts on marketing practices. The measure does include marketing restrictions, though Terry points out that more stringent requirements have been in place in recent years and enforcement likely will continue to rise. “They will have to revisit their tactics,” she says. “Warning letters were on the rise even before this reform. Last year, there were 108 warning letters, compared to 43 in 2008. Promotion-related fines are going to go through the roof.”

The legislation also will speed the biosimilars approval pathway in the domestic market. With a regulatory approval pathway in place in Europe and substantial guidelines to support biosimilar development, the European biosimilars market is significantly more advanced than the United States, where plans for a biosimilar regulatory approval pathway have stalled in recent years. “The biosimilars approval pathway is something we’ve known has been coming down the pike for many years now,” Terry says. “It’s available in Europe and there are guidelines in Canada, Japan and Australia. The U.S. is the last market to adopt this. Biosimilar manufacturers are going to be positively impacted, starting with those of the larger size. As well, large pharmaceutical companies with a large stake in this market will be positively impacted.”

Continued on page 41
MINNESOTA REP. KIM NORTON, D-ROCHESTER, says she actually sees Minnesota’s continued support of the Minnesota Partnership for Biotechnology and Medical Genomics as a way out of the state’s budget crisis, as the partnership has made considerable progress in its goal of making a positive economic impact on the state. “The state of Minnesota has said it is committed to exploring bioscience,” she says, “but we can’t just say we want to be a center of bioscience. We have to stick to it.”

“The investment we have made in the partnership is significant for a state our size, but it’s small when you compare it to investments in other states that are committed to scientific research,” Norton says. “Initially, we want there to be new research and new discoveries made, but we also want to be able to take these discoveries to the marketplace so we can have a positive economic impact on the state. If we can find new cures, drugs and devices, from a legislative standpoint, we’ll continue to invest in those parties if they have a positive economic impact. But we can’t just say we want to be a center of bioscience. We have to stick to it.”

MINNESOTA
CONTINUED FROM PAGE 38
To date, the partnership has submitted six papers for publication in prestigious medical journals; received equipment grants from the VA Medical Center Research Services and the Minnesota Medical Foundation; submitted two federal grant applications, including a competitive renewal of a National Institutes of Health (NIH) Specialized Programs of Research Excellence (SPORE) grant, and a National Science Foundation grant, and filed one patent application. Additionally, a partnership team is preparing to submit an application for an NIH Program Project Grant titled “Physical activity and obesity: From molecule to community.”

According to an economic quantification study of the partnership’s potential, a state investment of $70 million over five years, with mid-range assumptions, would yield an expected overall economic impact returned to the state of $830 million and 4,300 direct and indirect jobs in 2010.

REFORM
CONTINUED FROM PAGE 40
The Therapeutic Discovery Project Credit provides “an amount equal to 50 percent of the qualified investment for such taxable year with respect to any qualifying therapeutic discovery project,” which would permit some of the costs of preclinical research, clinical trials and other research protocols to be reduced, Gayle says. But the more important part of the legislation is the Approval Pathway For Biosimilar Biological Products, which permits biologics to maintain 12 years of market exclusivity after FDA approval.

“The biotechnology industry breathed a sigh of relief with this section’s passage because this clearly delineated time frame could have been much different,” Gayle says.

Not only that, Gayle adds, but the companies would also get a first look at any competitor that might be attempting to create a follow-on biologic. “Biotechnology companies developing reference therapeutics should be ecstatic with this section,” he says.

The top executives of two of Massachusetts’ largest biotechnology companies offered differing views recently during the annual meeting of the Massachusetts Biotechnology Council, a trade group.

“I don’t think this healthcare reform really addresses the fundamental underlying issues that are going to get after healthcare utilization,” James C. Mullen, CEO of Biogen Idec Inc. in Cambridge, Mass., told the annual meeting. He warned that U.S. healthcare will “look a lot like the European system,” where governments try to rein in costs through price controls on drugs and medical services.

Mullen, who is leaving Biogen Idec in June, also predicted biotech companies will face a more difficult regulatory process in the United States, the Boston Globe reported.

“The environment to launch new products... is going to be tougher, the pricing is going to be tougher, the probability of drug approvals is probably going to be more challenging,” he said.

According to Henri Termeer, CEO of Genzyme Corp. in Cambridge, Mass., the new law has the potential to boost investment in biotechnology research through a 12-year data exclusivity provision that shields biotech drugs from generic competition. The bill also contains a therapeutic-research tax credit for biotech start-ups. Unlike past pushes for health care overhaul that failed, “this particular set of discussions didn’t focus on the cost of innovation,” Termeer says. “It focused on the cost of access. In fact, you could say that innovation was somewhat talked about in a kind of benevolent way. There was support for the need to be able to take the risks that are necessary. This (Obama) administration is actually interested in innovation.”

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As some companies tighten their belts, CROs across the globe are enjoying this growing business trend

BY DAVID NUTTEN

Mid the choppy waters of the international economic seas in recent years, many pharmaceutical businesses have been tightening their belts to weather the stormy tide, and drug development has felt the pinch.

One sector of the industry has found itself swimming against the tide—contract research organizations (CROs), which have seen a steady increase in business over the last several years, tough financial times notwithstanding.

According to market research firm UBS Global Healthcare, the value of the global CRO industry is estimated at between $15 billion and $24 billion, with growth rates in the neighborhood of 15 percent annually. Biopharmaceutical companies spend $20.2 billion on drug discovery research annually, according to Barclays Capital, with $16.6 billion being outsourced today.

According to a 2005 Thomson CenterWatch survey, the $15 billion CRO industry was growing at a rate of 12 percent annually, but over the last two years, statistics point to a significantly greater rate of growth of nearly 17 percent.

In 2007, of the approximately $60 billion biotech and pharmaceutical companies spent on drug development, $35 billion, or about 25 percent, was outsourced.

In this story, the first in a multi-part series, we take an in-depth look at the geographical roots of outsourcing and where the business trend has spread, and we also examine the advantages and challenges of sending work outside your company’s walls—and potentially, your nation’s borders.

Where it all began

If you think the rise of CROs is a phenomenon that has taken off in the last five years, you would be mistaken.

Dr. J. Fred Pritchard, vice president of drug development services at Celerion in Lincoln, Neb., says CROs first emerged in the 1980s in North America in North Carolina, California, Pennsylvania and New Jersey areas, as well as Wisconsin, Texas and Nebraska.

“In Europe, CROs emerged in the major scientific centers of the United Kingdom, France, Germany, Netherlands and Switzerland, often evolving as spinouts of prior pharmaceutical operations,” Pritchard points out. “In Asia, CROs are emerging in India, China and there has always been some activity in Southeast Asia. Australasia, South Africa and South America have small industries by comparison.”

Pritchard says CRO locations are often dependent on the type of services they offer.

“Other factors include the need to have access to talent for recruitment into their organizations and being close to the client base,” he notes. “They are often close to major pharmaceutical or biotechnology hubs.”

Domestically, Pritchard notes that preclinical CROs tend to be located near areas that train people in veterinary sciences, while Phase I CROs are often located near areas that recruit volunteers successfully and also have a steady supply of scientifically trained workforce such as university centers. Late-stage clinical CROs have locations near major university clusters, such as Research Triangle Park in North Carolina, can feed the need for statisticians and medically trained professionals.

“Laboratory-based CROs need to consider transportation needs for efficiency as well as access to analytical chemists and bioengineers,” he says.

Drug discovery beyond borders

Officials with Amarex, a global CRO based in Germantown, Md., see outsourcing on the rise not only globally, but also on a domestic level.

Patrick J. Burke, senior director of business development at Amarex, says that domestically, the majority of CROs are located in regions of the country where the majority of drug development companies are located.

“One reason for locating near the drug development companies is that there are some advantages to the drug company being close to their vendor to facilitate communications, particularly to facilitate face-to-face meetings to review complex clinical trial projects,” says Burke. “It also benefits the CROs to work near the drug companies to give them access to a supply of trained employees that migrate between working for drug companies and CROs.”

According to Dr. Michael Schlosser, president and founder of Midwest BioResearch, most CROs are located in the United States, China and Japan, locating there because of access to major pharmaceuticals and biotech companies and to incur spending within region registering products, which is particularly important for China. Schlosser points out that in the United States, new CROs and expansion of existing CROs are tending to locate/expand in western areas (e.g., Covance, CRL) closer to biotech centers like San Diego and San Francisco.

Dr. Lee Babiss, executive vice president of global laboratory services at PPD Inc., a global CRO with offices in 41 countries, agrees that most large, global CROs have a strong presence in North America and Western Europe.

“Yet, they also have established operations in Asia, Eastern Europe and Latin America, three fast-growing, emerging markets where we are seeing strong growth in drug discovery and development,” Babiss says. “Clinical trials have become more complex and costly because of the need to satisfy stricter regulatory requirements and to ensure efficacious data. These regions have become increasingly important because they offer highly qualified investigators and large, targeted patient populations. For example, about 80 percent of Brazil’s residents live in urbanized areas, making patient enrollment, retention and post-trial communication easier.”

Advantages in key geographic areas

Burke notes that many CROs exist in the same region as their drug company partners because CRO founders may have worked for the companies in the past, and they start their business near where they live.

Accessibility to patients is an important consideration in order to enroll patients in clinical trials quickly. In addition, expansion into areas such as China and India has been occurring, driven by both cost efficiencies, which can be realized by both CROs and their clients, and access to well-educated and trained scientists.

“Our clients are expanding their programs into these areas because these regions offer large patient populations and well-educated, experienced investigators,” Babiss says. “China, for example, offers strong scientific talent. China’s pharmaceutical industry has experienced a 21 percent compounded annual growth rate over the past five years, and the drug discovery market is very strong. Asia Pacific is an important region for PPD, and an area where we have made long-term investments.”

Sekhar Medisetti, a healthcare analyst with GBI Research, says outsourcing is an attractive option for myriad companies because the time needed to recruit patients in Latin America continues to be very fast, leading to time and...
IN EUROPE, CROs emerged in the major scientific centers of the United Kingdom, France, Germany, Netherlands and Switzerland, often evolving as spinoffs of prior pharmaceutical operations.

IN ASIA, CROs are emerging in India, China and there has always been some activity in Southeast Asia, Australia, South Africa and South America have small industries by comparison.

—Dr. J. Fred Pritchard, vice president of drug development services at Celeron

notes that an in-depth understanding of the laws of all countries where trials are being conducted is required.

“As an example, when planning trials in Denmark, France, Portugal and Sweden, it is only necessary to apply to one ethics committee,” he says. “Yet, Germany, Spain and the Czech Republic have local ethics committees and a central ethics committee, and each give opinions on trial design and conduct, which can slow the start of a clinical trial.

Given today’s challenging R&D and regulatory environments, CROs also must understand that the needs of each client may vary. Medisetti cautions that CROs need to remain flexible, and use their global resources and technologies to deliver capabilities that bring both innovation and efficiencies to clients’ drug discovery and development programs.

“CROs that build close client relationships through strategic partnerships can become more closely involved earlier in a program and gain a better understanding of program goals,” he says. “When CROs work collaboratively with clients to deliver quality standards while meeting timelines and costs, clients want to continue to build upon that relationship.”

Regional hot spots

Looking to the future, PPD’s Babiss points out that biopharmaceutical companies will come to rely more heavily on the expertise, technologies and global resources of CROs to manage their R&D programs.

“CROs play a strategic role across all phases of drug discovery and development and can ensure patient safety, manage complex multinational trials and navigate changing regulatory environments,” he says. “We are also able to provide cost benefits and are more likely to have a deeper understanding of local language, culture and norms, qualities which lead to better relationships with investigators and improved trial execution.”

Schlosser believes that over the next few years, key emerging markets for CRO growth will likely be China and India.

“China and India are certainly poised for growth, however, as emerging quality starts to approach U.S. in these regions, prices which are already trending upward, which may limit the attractiveness for working in these regions by U.S. companies,” he says.

Medisetti, however, says he sees the potential for contraction in the CRO segment.

“I think that we are likely to see some consolidation because CROs will pursue mergers and acquisitions,” he says. “They will be looking for a chance to add services to their portfolios.”

For more information, visit www.DrugDiscoveryNews.com


IN EUROPE, CROs emerged in the major scientific centers of the United Kingdom, France, Germany, Netherlands and Switzerland, often evolving as spinoffs of prior pharmaceutical operations.

IN ASIA, CROs are emerging in India, China and there has always been some activity in Southeast Asia, Australia, South Africa and South America have small industries by comparison.

—Dr. J. Fred Pritchard, vice president of drug development services at Celeron

cost savings for companies, he explains.

“One reason that outsourcing is such an attractive option is the availability of a pool of available patients to participate in clinical trials,” Medisetti says. “Going forward, I see the shift to low-cost regions such as Eastern Europe and Latin American countries, Brazil and Mexico.”

Babiss says PPD’s acquisition of BioDuro, located in Beijing, enabled the company to offer preclinical small molecule drug discovery services to multinational and local clients.

“We gained more than 650 highly skilled chemists, biologists and quality scientists,” he says. “Combined with our acquisition of ExcelPharmastudies, we have expanded our capability to deliver global central laboratory, drug discovery, regulatory, Phase II-IV clinical development, data management and quality assurance services to biopharmaceutical companies in China, Japan and the entire Asia Pacific region. We are now the largest contract research organization to offer discovery and clinical development services in China.”

In Europe, CROs tend to be more regional in nature and cater to clients’ cultural and regulatory needs. Asian CROs are emerging quickly and offer lower costs; however, the industry is watching to see if they can consistently meet the rigors of western quality audits by sponsors and regulators, Pritchard adds.

“For European and North American clients, the time difference and distance can be a factor in ensuring good communications and oversight of the work,” Pritchard says.

Pitfalls and challenges

There are, of course, challenges facing outsourcing that can vary in certain geographic regions.

Jeremy Spivey, a senior research analyst at Cutting Edge Information (CEI), which recently produced a report on the outsourcing market, “While most companies see India and China as potential areas for large growth going forward, the perspective we heard is that they can still present problems if the trials aren’t managed extremely well. In some cases, regulatory hurdles or infrastructural issues can delay trials for many months. In North America and Europe, the cost of the CRO workforce is often high, so pricing tends to be increased on a per-patient or per-study basis,” Spivey adds. “However, other value-adds tend to be better, such as access to specific expertise, knowledge of the science, up-to-date equipment and methods of working.”

For some companies, even the most minor issues can become major when trials are running worldwide, according to CEI’s report.

“One top company realized they had a serious logistical issue when trial protocols were having to be translated into 33 different languages and dialects,” Spivey says. “Another found that the Spanish dialect used led to an improper protocol interpretation on a major element of the trial when read by those speaking a different dialect.”

Schlosser says other challenges impacting the outsourcing trend can include access to established CROs with depth of expertise, and the protection of intellectual property within the United States.

Burke agrees: “The biggest challenge is likely access to experienced staff, e.g., a region that might be very affordable in terms of living and business expenses is also likely to be a region without many people that have clinical research experience,” he says. “Another challenge would be a region that is not close to a sizable airport, because a certain level of periodic face-to-face meetings is important.”

Emerging regions do not have a long history of conducting clinical and development programs, and Babiss notes that there are sometimes immature infrastructures and facilities, unclear regulatory guidelines and ethics committees in hospitals that are not fully informed about good clinical practice (GCP) guidelines.

“Clients, CROs and regulatory agencies continue to put forth a large effort to increase GCP training and bring more scrutiny and adherence to GCP standards and standard operating procedures (SOP) in this region,” Babiss says. “In addition, China has a relatively long regulatory approval process, and it is working to bring regulatory filings more in line with the rest of world. Some of the best young talent, trained as chemists, is based in China. The challenge is that is takes several years of training to transition from a synthetic organic chemist to a medicinal chemist. While these challenges are real, the value PPD gains by making such investments will clearly be realized for our current and future clients and shareholders.”

In Europe, the Clinical Trials Directive was approved in 2001, although it was not fully implemented in most countries until 2006 and then only in the European Union. Babiss notes that the directive attempted to streamline clinical trials processes as multiple requirements made Europe a complicated area for drug development.

“While the directive has improved these processes, there continues to be problems with implementation in some countries,” he notes. “In addition, the clinical trials directive is only applicable to countries that are members of the European community. There are different processes for Eastern European countries such as Russia and the Ukraine.”

The Clinical Trials Directive was an important step toward creating uniform legislation in Europe, yet companies continue to face different requirements when conducting clinical trials in Europe, as there is not a unified approach to drug development. Babiss

Addition to antibody portfolio covering 6,900 human protein targets Sigma Life Science
Sigma Life Science, the biological products and services brand of Sigma-Aldrich, has added 2,200 new Prestige Antibodies powered by Atlas Antibodies to its portfolio, bringing the total Prestige Antibody portfolio to 8,300, covering 6,900 human protein targets, and expanding the company’s overall monoclonal and polyclonal antibody offering to more than 30,000. Prestige Antibodies are validated by the Human Protein Atlas (HPA) Program, a genome-wide program with a primary goal of producing a complete localization map of the human proteome that currently contains expression profiles and sub-cellular localization for close to 7,000 proteins. Each antibody is standardized in universal protocols with more than 700 immunohistochemistry, immunofluorescence and Western blot images per antibody, and all data is publicly available through the HPA.

Sigma Life Science
www.sigmaaldrich.com/life-science
(800) 240-4568

High-sensitivity laser scanning microplate cytometer for antibody discovery TTP LabTech
TTP LabTech has launched MirroMalt, a high-sensitivity laser scanning microplate cytometer for antibody discovery. MirroMalt performs mix-and-read, cell or bead-based assays. The instrument offers a solution to automated hybridoma screening and will not require the reworking of existing protocols. MirroMalt is also the first laser scanning microplate cytometer to offer simultaneous laser scanning. This will enable multiplexing resulting in higher throughput, single-pass scanning. The instrument is available in three upgradeable configurations; the highest specification will offer dual laser excitation (488 nm and 640 nm), four fluorescence data channels and a single laser scanner channel. MirroMalt’s laser scanner channel enables label-free object recognition independent of fluorescence, which can be combined with concurrent collection of fluorescence data for even greater sensitivity in multiplexed assays.

TTP LabTech
www.ttplabtech.com
(617) 494-9794

Plate-based, label-free biosensor SRU Biosystems
SRU Biosystems recently announced the extension of its product line of label-free instrumenta-
tion and biosensors with the introduction of its BIND Scanner, a plate-based, label-free instru-
ment capable of monitoring cellular responses at an individual cell resolution. The BIND Scanner has a compact design that allows it to be placed in a cell incubator to run assays at 37 degrees C and high humidity. Using new, modified micro-
plate-based photonic crystal biosensors, it can locate and track individual live cells with user-
controlled resolution (variable from 2 mm to 3.75 microns). It continuously monitors cell adhesion and morphological changes in real-time, allowing assays to be run using small popula-
tions of cells, or even single cells. BIND biosen-
sor microplates are compatible with standard fixation and staining techniques, including fluo-
rescence applications, allowing orthogonal infor-
mation to be gathered by the user. The BIND system supports the use of 8, 16, 384- and 1,536-well microplates using the company’s optical biosensor technology.

SRU Biosystems
www.srubiosystems.com
(781) 933-7255

System combined TOF mass spectrometers and high-throughput processing speed BIOCIUS Life Sciences
The RF360 Hi-Res System from BIOCIUS Life Sciences and Agilent Technologies combines the mass capabilities of Agilent’s time-of-flight mass spectrometers and the high-throughput processing speeds of RapidFire technology from BIOCIUS. RF360 combines the sample processing speed of RapidFire with high resolution TOF/MS, eliminat-
ing the lengthy method development required for the analysis of metabolic stability, PK/PhC, and other in vitro ADME assays. RF360 processes at ~10 seconds per sample, up to 10 times faster than LC-based methods, without any compromise in data quality.

BIOCIUS Life Sciences
www.biocius.com
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Biological assessment cartridges Thermo Fisher Scientific Inc.
Thermo Fisher Scientific Inc. introduces three new biological assessment cartridges for the Thermo Scientific Celomics™ Tofspec in vitro (iVT) toxicology platform. The ToxInsight iVT platform advances drug discovery and development by enabling multiple toxicity assessments on a cell-by-cell basis. The platform includes automated cell imaging, instrumention, software and reagent car-
ttridges with prevalidated panels for toxicity assess-
ment targets. Tier I panels allow rapid profiling of multiple simultaneous toxicity endpoints, while Tier II follows with single endpoint assays to determine mechanism of action.

Thermo Fisher Scientific
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(781) 622-1000

Oligo panels for qPCR Biosearch Technologies
Biosearch Technologies Inc. announced that the company has introduced ValuPanel Reagents, a new product line of oligo panels for qPCR that contain probes and primers to resolve the genet-
ic signatures of a variety of influenza strains. The influenza ValuPanel Reagents include the previ-
ously announced signatures for H5N1 viral strains, as well as a novel set associated with influenza A subtypes. The Influenza A Subtyping ValuPanel Reagents comprise oligos based on the following seven signature sequences: universal strain of influenza A; influenza A H1 subtypes; influenza A H3 subtype; influenza A H5a subtype; influenza A H5b subtype; universal strain of influenza B and influenza B H1 subtype as a positive control.

Biosearch Technologies
www.biosearch.com
(908) 722-5000

Large tube clamp Advanced Scientifics
Advanced Scientifics has developed a large tube clamp to control or stop the flow of the fluid through a variety of tubing from OD to 1 OD (1/8-inch wall). The component is com-
prised of a simple, secure locking and unlocking feature for versatility. Typical appli-
cations of the clamp include biopharmaceutical manufacturing and pharmaceutical processes; disposable filtration systems; mixing containers and vessels; assem-
bles; and tubing sets.

Advanced Scientifics
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vative µArray custom microarray platform forms a comprehensive service package tailored to your specific research needs. Following exploratory sequencing of small RNA and extensive bioinformatic analysis, which defines the comprehensive set of sequences, microarray probes are designed and efficient profiling on custom microar-
rays is performed.

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Hamamatsu’s new FDSS µCELL is a small, afford-
able plate reader that dispenses and images 96 or 384-well microplates for kinetic cell-based assays. This simple-to-use plate reader gets results fast by imaging the entire plate. Applications include GPCR assays, ion channel assays, prolyl isomerase and other enzymatic assays, trans-
porter assays and light-activated receptor or channel assays.

Hamamatsu Corp.
http://sales.hamamatsu.com/info/fdss/
(800) 524-0004

Stand-alone microCT system for preclinical imaging
Caliper Life Sciences Inc.
Caliper Life Sciences Inc. recently launched the Quantum FX, a stand-alone microCT system for preclinical imaging. The Quantum FX is a low-dose, microCT system that provides researchers with a 3D anatomical view of disease activity, tumor development and therapeutic response over mul-
tiple time points during the course of a study. Quantum offers complementary 3D anatomical precision for current imaging applications, while also expanding Caliper’s offering in areas includ-
ing skeletal, vascular and respiratory disease. It uses ultra-fast, sensitive and low dose CT technology to create high-resolution 3D images with minimal X-ray exposure.

Caliper Life Sciences
www.calipers.com
(508) 435-9500

New products

For more information, visit www.DrugDiscoveryNews.com
Brody as the new chief of its Genome Technology Branch (GTB), the largest of seven branches in the NHGRI Division of Intramural Research. Brody has headed GTB’s Molecular Pathogenesis Section and serves as chief scientific officer of the Center for Inherited Disease Research, an NHGRI-affiliated facility operated by Johns Hopkins University in Baltimore, Md.

Harlan Laboratories Inc.

Hans Thunem
CEO
INDIANAPOLIS—Contract research organization Harlan Laboratories Inc. has named its former group president of research models and services business, Hans Thunem, as the company's new CEO and as a board member. Thunem has held senior management positions in the oil, high technology and life sciences industries and, prior to joining Harlan, Thunem was CEO at Lifelabs, Canada's largest private sector medical diagnostics provider.

Stratos Genomics

Heiner Dreismann, Ph.D.
Director
SEATTLE—Stratos Genomics Inc. has announced the addition of former Roche Molecular Diagnostics CEO Dr. Heiner Dreismann to its board of directors. Dreismann is recognized as a driving force behind molecular biologists’ adoption of the polymerase chain reaction (PCR) technique in the 1990s for use in basic research and drug discovery laboratories. While heading up Roche Molecular Diagnostics, Dreismann led the development and commercialization of an expansive portfolio of PCR products. Dreismann has held other senior positions within Roche in the areas of global business development, including business unit manager for PCR and microbiology, as well as in manufacturing and research and development for microbiology and infectious diseases.

Silence Therapeutics

Max Herrmann
Chief Financial Officer
LONDON—Silence Therapeutics plc has appointed Max Herrmann as the company’s chief financial officer and company secretary. Herrmann has more than 20 years of biotechnology and pharmaceutical industry experience, having held key management positions with leading development stage companies, as well as several investment banks. He served most recently as CFO of Intercytex PLC, a publicly traded company focused on the emerging area of regenerative medicine. Before joining Intercytex, he spent more than 10 years as a sell-side equity analyst, most recently as managing director and head of European pharmaceutical and biotechnology research at ING. Herrmann also worked in the United States as financial controller for Onyx Pharmaceuticals Inc., where he was involved in the company’s successful initial public offering on NASDAQ.

Talen Therapeutics

John Maraganore, Ph.D.
Director
CAMBRIDGE, Mass.—Talen Therapeutics, a biotechnology company developing therapies around inflammatory and immune diseases, has appointed Dr. John Maraganore, CEO of Alyxan Pharmaceuticals, to its board of directors. Maraganore joined Alyxan in December 2002. Prior to Alyxan, he served as an officer and senior vice president of product development at Millennium Pharmaceuticals, in senior roles at Biogen Inc. and in scientific management positions at Zymogenetics Inc. and the Upjohn Co. Maraganore is chairman of Regulus Therapeutics and a director of Archexim and Macrogenetics. He is also a member of the Research Advisory Board of the Beth Israel Deaconess Hospital.

Sanford-Burnham Medical Research Institute

Kristiina Vuori, M.D., Ph.D.
President
LA JOLLA, Calif.—Sanford-Burnham Medical Research Institute has promoted Dr. Kristiina Vuori to president of the institute. In this role, she will oversee Sanford-Burnham’s day-to-day operations. Prior to the promotion, Vuori was executive vice president of scientific affairs. She will continue to manage her cancer research laboratory and remain director of Sanford-Burnham’s National Cancer Institute-designated Cancer Center.
REPORT CALLS DRUG SAFETY ‘the brakes of the pharmaceutical car’

DURHAM, N.C.—You would drive a car with a dent in it, or even a cracked windshield, but you would never drive a car without the brakes working properly. This sentiment illustrates the tremendous importance of pharmaceutical drug safety teams to the process of producing effective medications, according to a recent Cutting Edge Information (CEI) report, “Benchmarking Drug Safety and Pharmacovigilance.”

Compiling and analyzing more than 30 sets of data from pharmaceutical and biotechnology companies of various sizes, CEI notes that by monitoring the drugs’ serious and non-serious adverse effects from their earliest testing in humans through their post-marketed lifecycle, drug safety teams can help prevent harm to patients by quickly recognizing products’ side effects and dealing with them, up to and including pulling drugs from shelves.

“In many documented cases, drug safety teams have uncovered serious adverse effects—sometimes even fatal ones—and quickly acted to address the issues and continue to save lives,” the report notes. “These groups can also save pharmaceutical companies millions of dollars in the long run.”

According to CEI’s findings, in clinical testing, drug safety teams might initially identify a series of adverse effects, but further analysis shows that the effects are specific to a certain patient population or to those with certain health conditions. This kind of discovery can allow products to continue on to market, with risk management plans to prevent certain patient groups from receiving the medication. Without an organizationally mature drug safety group to manage and study the adverse effects, some companies may steer clear of launching such a drug, resulting in the loss of tens or hundreds of millions of dollars, without a product to recoup development costs.

Percentage of companies with in-house teams to manage drug safety/pharmacovigilance

Phase in which drug safety activities begin

Percentage of drug safety budget outsourced by company

Percentage of drug safety groups performing activities

ABOUT CUTTING EDGE INFORMATION
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