BIOWORLD™ TODAY

THE DAILY BIOPHARMACEUTICAL NEWS SOURCE

APRIL 30, 2015 | BIOTECH'S MOST RESPECTED NEWS SOURCE FOR MORE THAN 20 YEARS | VOLUME 26, NO. 83

THUMBS UP, WITH SOME CAVEATS

Amgen's pioneering immunotherapy gets FDA adcom support

By Mari Serebrov, Regulatory Editor

Despite the challenges of being a biologic pioneer, Amgen Inc.'s melanoma drug, talimogene laherparepvec, or T-vec, garnered the support of two FDA advisory committees – with some caveats.

See Amgen, page 3

FINANCINGS

Crispr Therapeutics spices up genome editing competition with $64M in new cash

By Cormac Sheridan, Staff Writer

DUBLIN – Crispr Therapeutics AG raised $64 million in new funding, bringing in two heavyweight strategic investors, London-based Glaxosmithkline plc,

See Crispr, page 4

REGULATORY

Subcommittee releases version 2.0 of 21st Century Cures draft

By Mari Serebrov, Regulatory Editor

After months of bipartisan negotiations, a House subcommittee yesterday released its 2.0 discussion draft of the 21st Century Cures Act that fills one of the holes in the first version released in January – provisions to bolster funding

See Cures, page 5

IN THE CLINIC

Beigene discloses science behind its three phase I cancer candidates

By Shannon Ellis, Staff Writer

SHANGHAI – Beigene Co. Ltd. has three candidates currently in phase I trials in Australia and has revealed the science and possible indications behind the cancer compounds: BGB-283, a second

See Beigene, page 6

FINANCINGS

Sanbio IPO raises $67M to carry stroke therapy forward

By Michael Fitzhugh, Staff Writer

Sanbio Co. Ltd., a small trans-Pacific cell therapy company leveraging Japan's efforts to foster regenerative medicine development, has completed an IPO of shares (TYO:4592) on the Tokyo Stock

See Sanbio, page 7

REGULATORY

Chin fat reduction drug Kybella gets FDA nod ahead of PDUFA date

By Peter Winter, BioWorld Insight Editor

Not unexpectedly the FDA gave the green light to Kythera Biopharma Inc.'s fat reduction drug Kybella (deoxycholic acid), as a treatment for adults with moderate-to-severe fat below the chin,

See Kythera, page 8

THE BIOWORLD BIOME

TAKING OUT T790M

Targeted agents best T790M mutation in non-small-cell lung cancer

By Anette Breindl, Senior Science Editor

Two concurrently published papers showed yesterday that patients with the T790M resistance mutation responded at high rates to either rociletinib (CO-1686,

See NSCLC, page 9

IN THE CLINIC

PHASE II ENROLLING FAST

Tyrogenex seeks APEX of wet AMD treatment, advancing oral X-82

By Jennifer Boggs, Managing Editor

With the goal of providing the first oral option for patients with wet age-related macular degeneration (AMD), Tyrogenex Inc. launched a phase II study of X-82,

See Tyrogenex, page 10

ALLICENSE 2015

Not-for-profits seeking stronger partnerships in return for early dollars

By Marie Powers, News Editor

In the heady days when venture capital (VC) was flowing like a waterfall, not-for-profit support of biotech endeavors was considered – by both parties – as a type of gravy, sometimes with the end goal of

See Allicense, page 11

FINANCINGS

GW Pharmaceuticals plc, of London, said it priced an underwritten public offering of 1.6 million American Depositary Shares (ADSs), representing 19.2 million ordinary shares of the company, at $112 per ADS on the Nasdaq Global Market, raising gross proceeds of approximately $179.2 million. The company has granted the underwriters a 30-day option to purchase up to an additional 240,000 ADSs at the public offering price. Morgan Stanley, BofA Merrill Lynch and Cowen and Co. are acting as joint book-running managers for the offering. Piper Jaffray & Co. is acting as lead manager.

Novogen Ltd., of Sydney, Australia, said it completed the placement to U.S. institutional investors of 51.75 million ordinary shares, raising a total of $15.525 million. Subject to shareholder approval, the company will issue 51.75 million unlisted options exercisable at $0.30 within six months from the date of issue and 25.875 million unlisted options exercisable at $0.40 within five years from the date of issue. The funds will be applied to bringing a pipeline of three oncology drugs (Cantrixil, Trilexium, Anisina) through the clinic to the point intended to test their ability to provide a meaningful clinical benefit to patients with abdominal cancers (malignant ascites), adult and pediatric brain cancers, neuroblastoma, malignant melanoma and castrate-resistant prostate cancer. In the non-oncology space, the programs of ulcerative colitis, repair of brain and spinal injury, the treatment of muscular dystrophies, and the treatment of lysosomal storage diseases will all now be moved into active phases, the company said, with the intention of identifying at least three candidate drugs to be made clinic-ready within two years.

Pamlico Biopharma Inc., of Oklahoma City, said it completed a $2.2 million series A equity financing led by Accele Venture Partners, the investing arm of life sciences accelerator Accele Biopharma, and the Oklahoma Seed Capital Fund, managed by I2E Inc. Proceeds will be used to advance the company's research and development of human antibody therapeutics and diagnostics for infectious diseases and cancer. Pamlico's lead clinical candidate, Pneumomab, is a mixture of serotype-specific human monoclonal antibodies against *Streptococcus pneumoniae* (SPN). It is in preclinical development for the treatment of severe community-acquired pneumococcal pneumonia (SPN-CAP).

Viking Therapeutics Inc., of San Diego, said it priced its IPO of 3 million shares at $8 per share. The company has granted the underwriters a 30-day option to purchase up to an additional 450,000 shares of common stock at the same price to cover overallotments, if any. Viking expects the shares to begin trading on the Nasdaq Capital Market under the ticker symbol VKTX. The company has exclusive worldwide rights to a portfolio of five therapeutic programs in clinical trials or preclinical studies, which are based on small molecules licensed from **Ligand Pharmaceuticals Inc.**, of San Diego, which invested $9 million in the offering.

STOCK MOVERS 4/29/2015

Company	Stock in $	Change in %
Nasdaq Biotechnology	-$0.30	-0.01%
Bio-Path Holdings, Inc.	+$0.40	+29.41%
Paratek Pharmaceuticals	-$2.52	-9.12%
Spark Therapeutics Inc.	+$5.32	+9.56%
Plasmatech Biopharma	-$0.47	-14.51%

Biotechs showing significant stock changes Wednesday

BIOWORLD TODAY

BioWorld™ Today (ISSN# 1541-0595) is published every business day by Thomson Reuters, 115 Perimeter Center Place, Suite 1100, Atlanta, GA 30346 U.S.A.

OUR NEWSROOM

Atlanta - Lynn Yoffee (News Director), Jennifer Boggs & Amanda Lanier (Managing Editors), Peter Winter (BioWorld Insight Editor), Karen Pihl-Carey (Database Editor), Ann Duncan (Senior Production Editor), Marie Powers (News Editor), Randy Osborne (Staff Writer) // **East Coast** - Anette Breindl (Senior Science Editor), Mari Serebrov (Regulatory Editor) // **West Coast** - Michael Fitzhugh (Staff Writer) // **Europe** - Nuala Moran & Cormac Sheridan (Staff Writers) // **Asia:** John Fox, Shannon Ellis, Catherine Makino, Alfred Romann, Dave Silver, Cornelia Zou (Staff Writers)

PRACTICAL INFORMATION

For Sales Inquiries: http://ip-science.interest.thomsonreuters.com/Bioworld_Sales_Inquiry. NORTH AMERICA, Tel: +1-855-260-5607. Outside of the U.S. and Canada, Tel. +44-203-684-1797. For Customer Service Inquiries, NORTH AMERICA, Tel: +1-800-366-4474. Outside of the U.S. and Canada, Tel. +44-203-684-1796.

For ad rates & information, contact Tyler Beatty toll free at (855) 260-5607 or, outside the U.S. and Canada, at (646) 822-4549, email tyler.beatty@thomsonreuters.com.

For photocopy rights or reprints, please contact Tyler Beatty toll free at (855) 260-5607 or, outside the U.S. and Canada, at (646) 822-4549, or by email at tyler.beatty@thomsonreuters.com.

Send all **press releases and related information** to newsdesk@bioworld.com.

BUSINESS OFFICE

Donald R. Johnston (Senior Director, Editorial), Sarah Cross (Marketing Director), Penney Holland (Web Production Manager), Tracie Webb (Customer Service Manager)

CONTACT US

Jennifer Boggs, (770) 810-3120 // Anette Breindl, (770) 810-3134 // Sarah Cross, (770) 810-3138 // Michael Fitzhugh, (770) 810-3064 // Penney Holland, (770) 810-3047 // Donald R. Johnston, (770) 810-3118 // Nuala Moran, 44-7778-868-579 // Randy Osborne, (770) 810-3139 // Marie Powers, (770) 810-3136 // Mari Serebrov, (770) 810-3141 // Cormac Sheridan, 353-87-6864323 // Tracie Webb, (770) 810-3130 // Peter Winter, (770) 810-3142 // Lynn Yoffee, (770) 810-3123

Amgen

Continued from page 1

The Cellular, Tissue and Gene Therapies and Oncologic Drugs Advisory Committees voted 22-1 Wednesday that T-vec's overall risk-benefit profile supported traditional approval for the treatment of injectable, regionally or distantly metastatic melanoma.

It was the wording of the indication for the first-in-class oncolytic immunotherapy that drew the lone no vote and several of the caveats.

The data were clear, but the FDA's question was muddy, said Richard Sherry, a staff clinician at the National Cancer Institute. His concern was the broadness of the patient population represented in the indication when the data showed T-vec had the most significant effect in stage III and IVa melanoma.

"This is a chance to make a statement," he said. "This drug is not appropriate for the vast majority of patients with visceral disease."

Patrick Hwu, a melanoma professor at the University of Texas M.D. Anderson Cancer Center, supported approval without limiting the patient population. "I need as many arrows as possible in my quiver" to better treat patients, he said, noting that T-vec is among the least toxic cancer agents.

While he wouldn't use it blindly on patients, Hwu said he has patients he would treat with the drug. "Let physicians be professionals and make the best decisions" for their patients, he added.

Sherry shot back that no one outside the FDA and advisory committees will look at the clinical trial data to see which patients truly benefitted from T-vec.

While several other panelists agreed with Sherry that T-vec should be restricted to melanoma patients without visceral disease, they voted yes on approval. However, they recommended labeling restrictions and education programs for oncologists and patients.

Like Hwu, panelist Louis Diehl, a professor at Duke University Medical Center, voted an unequivocal yes, saying the patient testimony during a public hearing helped him focus on the benefit of the drug. Given how T-vec saved the patients' lives when their doctors had given up hope, he said he wouldn't want to take the drug out of the hands of oncologists or restrict its use to certain patient subgroups.

If approved, T-vec would be only the second therapeutic cancer vaccine approved by the FDA and the first approved to treat melanoma. But for panelist Grzegorz Nowakowski, an assistant professor at Mayo Clinic, the drug is just another modality in the oncologist toolbox. As a single agent, he doesn't think it will change the melanoma field, which has seen the approval of a number of new therapies since the phase III T-vec trial started in 2008.

Going forward, Hwu said, Amgen needs to look at T-vec in combinations, especially with some of the newer melanoma drugs.

In the briefing documents released before the adcom meeting, the FDA struck a critical tone, noting that T-vec showed a "strong trend" but missed statistical significance in overall survival (OS) in the phase III study in metastatic melanoma. Although OS was a secondary endpoint and T-vec met the primary endpoint of durable response rate in the randomized, open-label OPTiM trial, the FDA's penchant for a strong OS benefit is well known in the cancer community. (See *BioWorld Today*, April 28, 2015.)

Since T-vec is derived from an attenuated herpes simplex virus-1 isolate, the FDA also raised concerns about the potential for viral shedding and transmission. While the committees spent considerable time discussing the possibility, the panelists didn't seem overly concerned, describing it as low risk. Amgen is conducting a shedding study to shed more light on the issue.

The Thousand Oaks, Calif.-based company acquired T-vec, then known as Oncovex, in its $1 billion buyout in 2011 of Biovex Group Inc. (See *BioWorld Today*, March 21, 2013.) //

OTHER NEWS TO NOTE

Aequus Pharmaceuticals Inc., of Menlo Park, Calif., and **Corium International Inc.**, of Vancouver, British Columbia, said they entered an agreement under which the parties might co-fund new transdermal products with an initial focus on neurological disorders. Under the terms, for each product selected for development the parties will assign an allocation of responsibilities, costs, rights and product revenues. Specific financial terms were not disclosed. The deal builds upon the progress made under the feasibility and preclinical development agreement entered into in May 2014 focusing on Aequus' lead program, AQS-1301, a transdermal aripiprazole product candidate in development for potential weekly use in the treatment of irritability associated with autistic disorder, bipolar I disorder, schizophrenia and major depressive disorder. Under that earlier agreement, Corium's transdermal technology was incorporated into AQS-1301, providing Corium with an economic interest in the program and the option to further increase its interest by co-funding clinical development. Aequus has exclusive worldwide rights to AQS-1301 and intends to seek third-party partners to commercialize that program in the U.S., Europe and Asia, while retaining the commercial rights for Canada.

AKL Research & Development Ltd. said it is relocating to Stevenage Hertfordshire, UK, and will be based at the Stevenage Bioscience Catalyst. AKL said the decision to move was based on finances and tax credits. The company is developing synthetic drugs derived from natural products where anti-inflammatory activity has been shown.

Crispr

Continued from page 1

through its SR One venture capital arm, and Celgene Corp., to advance its development of novel therapies based on Crispr-Cas9, the genome editing technology that has taken the academic world by storm since its emergence in 2012.

The new funding came in two separate transactions. SR One led a $35 million second closing of the company's series A round, which also included New Enterprise Associates and Abingworth. "We had a very significantly oversubscribed series A extension," Crispr Therapeutics CEO Rodger Novak told *BioWorld Today*. "We really had to send lots of people away."

But one doesn't normally do that when Summit, N.J.-based Celgene comes calling. Moreover, there was already an existing matrix of relationships between the two organizations. Novak and Celgene's head of business development, George Golumbeski, had previously worked together at Nabriva Therapeutics AG, of Vienna.

And Celgene also has a close relationship with San Francisco-based Versant Ventures, the founding investor of Crispr Therapeutics. Earlier this week, it agreed a potential $485 million buyout of Versant's first build-to-buy firm Quanticel Pharmaceuticals Inc., of San Francisco, after an ongoing collaboration in oncology. (See *BioWorld Today*, April 28, 2014.)

"It was clear that Celgene was interested, so we discussed what we would do," Novak said. The upshot of that was a $29 million series B round and the opportunity to plug into that company's extensive expertise in oncology and beyond.

Having raised $89 million in total, the Basel, Switzerland-based company is now the most heavily funded of the mini-cluster of start-ups formed during the last 18 months with the aim of translating the enormous promise of the technology into clinical applications.

The new cash will give it a generous financial cushion as it continues its preclinical R&D work – its first trials are about three years off still – and enough firepower should any legal costs arise from an ongoing patent battle concerning the invention of the technology. "We feel very comfortable and strong about our IP position," said Novak.

Lined up on one side of the dispute are Crispr founder Emmanuelle Charpentier, of the Helmholtz Center for Infection Research, in Braunschweig, Germany, and Jennifer Doudna, of the University of California, Berkeley, who is associated with Cambridge-based Intellia Therapeutics Inc., which recently closed a $15 million series A round with Atlas Ventures and Novartis AG. On the other is Editas Medicine, also of Cambridge, whose founders include Feng Zhang, of the Broad Institute, who received the first granted patent on Crispr-Cas9, and George Church, of Harvard University. Although also a founder of this firm, Doudna has recently severed her links with it.

"Intellia and us – we have the foundational IP," Novak said. Given the scale of the opportunity there will be room for more than one player, he said. "I'm sure, over time, we'll find a solution that's acceptable to all the parties involved," he added.

None of those developing Crispr-based therapies has divulged details of their lead programs as yet, but these are expected to focus on ex vivo manipulation of cells initially. The main issue in translating the technology is the age-old one. "The biggest challenge is to have an efficacious intervention," Novak said. Knocking out a gene is, in itself, not difficult, for example, but it's only a start. "Is it sufficient to change the course of pathology of a disease?" he asked.

The other dimensions of the challenge are not a whole lot different from those associated with regular drug development. "Once you're efficacious, sure, you need to make absolutely sure you're safe and you have an industrial process."

The recent controversy arising from the online publication in *Protein & Cell* of a paper from a Chinese group describing the first attempts at human germline modification with Crispr-Cas9 is "a total distraction," Novak said. "We do need a discussion around these things. We will see more papers like this – the discussion has just started."

Crispr Therapeutics, Intellia and Editas are all adamant that their focus is on somatic cells only – and steering such programs through preclinical and clinical development is more than enough work as it is. //

OTHER NEWS TO NOTE

Amarantus Bioscience Holdings Inc., of San Francisco, said the European Commission granted orphan drug status for MANF (mesencephalic-astrocyte-derived neurotrophic factor) for the treatment of retinitis pigmentosa (RP). The company previously received orphan drug designation for MANF for the treatment of RP from the FDA.

Amgen Inc., of Thousand Oaks, Calif., said the FDA's Endocrinologic and Metabolic Drugs Advisory Committee (EMDAC) will review data supporting its biologics license application (BLA) for Repatha (evolocumab) for the treatment of high cholesterol at a meeting on June 10. The investigational fully human monoclonal antibody inhibits proprotein convertase subtilisin/kexin type 9 (PCSK9), a protein that reduces the liver's ability to remove low-density lipoprotein cholesterol (LDL-C) from the blood. Data in support of the BLA come from approximately 6,800 patients, including more than 4,500 patients with high cholesterol in 10 phase III trials that evaluated the safety and efficacy of Repatha in patients with elevated cholesterol, including patients on statins with or without other lipid-lowering therapies; patients who cannot tolerate statins; patients with heterozygous familial hypercholesterolemia and patients with homozygous familial hypercholesterolemia. The FDA has set a PDUFA date of Aug. 27, 2015.

Cures

Continued from page 1

for the National Institutes of Health (NIH).

The bill calls for nearly $32 billion for NIH for fiscal 2016, $33.3 billion for fiscal 2017 and close to $35 billion for fiscal 2018. In addition, it would establish a $2 billion NIH Innovation Fund to be used for precision medicine, young emerging scientists and other areas that have yet to be spelled out. It also creates more accountability at the NIH, while easing some of the administrative burdens that currently hamper the institutes.

The draft legislation came a day before the one-year anniversary of the 21st Century Cures Initiative, which has included a series of roundtables, hearings and town hall meetings convened to gather ideas on how to bridge the gap between scientific and medical advances and the regulation of new therapies.

The new draft will be the center of conversation today when the Energy and Commerce Subcommittee on Health holds another hearing to get feedback from the FDA and NIH. The next steps will be to finalize the bill and garner broad support for its passage. Subcommittee Chairman Fred Upton (R-Mich.) intends to have a final bill on the president's desk by the end of the year.

The initiative aims to strengthen the development of new drugs and devices, improving the transition from basic science to development and development to delivery, according to the subcommittee. One of the big targets is the development of cures for thousands of diseases with no approved therapies.

The draft includes provisions to:

• incorporate the patient perspective into the development process;

• foster the development, qualification and utilization of biomarkers;

• modernize clinical trials;

• facilitate the development of the next line of antibiotics;

• provide incentives for repurposing drugs for serious and life-threatening diseases and disorders;

• provide clarity for developers of software products used in health management and medical care;

• unlock the wealth of available data to further research and innovation;

• unleash the promise of personalized medicine.

At 199 pages, the new draft is about half the size of the one released earlier this year, but a lot of placeholders have yet to be filled in. Democrats on the subcommittee refused to endorse the 1.0 version, because it included no increased funding for the NIH – something Rep. Frank Pallone (D-N.J.) said was a common theme during the public engagement, from both sides of the aisle. More NIH funding "is fundamental to truly advancing 21st century cures," he added. (See *BioWorld Today*, Jan. 29, 2015.) //

OTHER NEWS TO NOTE

Ariad Pharmaceuticals Inc., of Cambridge, Mass., said it has reached a settlement agreement to end its proxy fight with Sarissa Capital Management. Ariad's founder, Harvey J. Berger, said he will retire as chairman and CEO, effective Dec. 31, or when a successor has been named. Alex Denner, of Sarissa Capital, has been named chairman of a search committee to find a new CEO. Under the settlement agreement, Ariad appointed Anna Protopapas to its board and Sarissa is withdrawing its proposed slate of names to be added to the board.

Biogen Inc., of Cambridge, Mass., and **Abbvie Inc.**, of North Chicago, said the FDA accepted for review the companies' biologics license application for Zinbryta (daclizumab high-yield process) for relapsing-remitting multiple sclerosis (MS). The drug, a new form of a humanized monoclonal antibody, is designed to selectively bind to the high-affinity interleukin-2 receptor subunit (CD25) that is expressed at high levels on T cells that become abnormally activated in MS. Zinbryta also is under review in Europe.

China Cord Blood Corp., of Hong Kong, said it has formed a special committee from its board to consider a proposal from **Golden Meditech Holdings Ltd.**, of Hong Kong, to acquire all outstanding ordinary shares of the company not already owned by Golden Meditech in a deal to take the company private. Three independent directors have been appointed to the committee, which will be chaired by Mark D. Chen. (See *BioWorld Today*, April 29, 2015.

Evotec AG, of Hamburg, Germany, and **Facio Therapies BV**, of Leiden, the Netherlands, said they entered an agreement aimed at the identification of compounds showing activity as potential treatments to stop the progression of facioscapulohumeral dystrophy (FSHD), a muscle wasting disease. The project entails the setup and execution of an automated high-throughput screen to identify small molecules having a positive effect on SMCHD1 and DUX4 activity in human FSHD-affected muscle cell lines. The compounds that show promising activity in that screen are expected to be available in the first half of 2016 for further testing to produce compounds that are suitable for the development of a therapeutic for the treatment of FSHD. Financial terms of the collaboration were not disclosed.

Green Cross Corp., of Yongin, South Korea, said it plans to build a new cell therapy manufacturing facility at the Guian New Area in the Guizhou province of China. The new manufacturing site sets to address the cellular therapeutic industry's demand for clinical studies and commercial supply.

Northern Biologics Inc., of Toronto, said it entered a collaborative agreement with **Celgene Corp.**, of Summit, N.J. Northern Biologics received $30 million up front and will use the funding for discovery and development of first-in-class therapeutic antibodies in oncology and fibrosis, and has the right to receive additional payments to advance its portfolio. Celgene has options to in-license drug candidates and also has the right to acquire Northern Biologics at the end of the collaboration.

Beigene

Continued from page 1

generation inhibitor of B-RAF; BGB-290, a poly (ADP-ribose) polymerase (PARP) inhibitor and BGB-3111 inhibitor of Bruton tyrosine kinase (BTK).

Beigene had seven posters at the recent American Association for Cancer Research. The abstract, titled "BGB-283, a novel RAF kinase and EGFR dual inhibitor, displays potent antitumor activity in B-RAF mutated colorectal cancers," was selected as an oral presentation.

"This is the first time we disclosed the molecular profile for BGB-283," Lusong Luo, head of discovery biology of Beigene, told *BioWorld Today*.

Beigene has found that BGB-283 is a second-generation inhibitor that inhibits not only RAF kinases, but also the EGFR, citing data from preclinical biochemical level, cellular level and in vivo xenograft models. Additionally, Beigene presented findings suggesting that combining RAF dimer inhibitor BGB-283 and MEKi could be a strategy to treat RAS mutated cancers.

According to Luo, these findings support BGB-283 as a potent antitumor drug candidate with clinical potential for treating colorectal cancer (CRC) harboring B-RAFV600E mutation.

BGB-283 is part of a two-candidate development deal that Beigene signed with Merck Serono, a division of Merck KGaA, in 2013, valued at approximately $515 million that gives Merck ex-China rights to both BGB-283 ($283 million) and BGB-290 ($232 million). Under the agreement, Beigene is responsible for development and commercialization in China.

BGB-283 enrolled its first patient in December 2013, and in May 2014, Beigene received a $5 million milestone payment from Merck.

The second candidate in the Merck deal, BGB-290, is a PARP inhibitor that, Luo said, is highly selective for PARP-1 and PARP-2 with very good DNA trapping activity.

But unlike most PARP inhibitors, BGB-290 has shown strong blood-brain barrier penetration, which opens up the possibility of being effective for brain tumors.

"The brain vs. plasma is 20 percent; that is very good and gives us the potential to work in glioblastoma," said Luo.

BGB-290 also demonstrated strong synergism with temozolomide, a chemotherapy drug for brain tumors and for non-small-cell lung cancer (NSCLC) with brain metastasis, in subcutaneous and intracranial xenograft models.

This candidate dosed the first patient in July 2014 and triggered a $9 million payment to Beigene two months later as part of the Merck deal.

THE PDX ADVANTAGE

These early studies have made use of Beigene's patient biopsy-derived xenograft (PDX) platform. The company has said that their PDX models allow them to work on primary or recurrent tumors at a relevant stage of tumor progression affording better clinical prediction than surgical samples. The company has ready access to patient tumors, and stated their SCLC primary tumor models came from patient samples obtained from the Beijing Cancer Hospital.

Earlier this month, John Oyler, CEO of Beigene, spoke at the China Healthcare Investment Conference in Shanghai, sharing his company's strategy to go after combination solutions in immuno-oncology and targeted agents, calling this the future oncology. He also credited the company's translational success in part to its biopsy-derived xenograft platform for providing tools for compound differentiation into best or first-in-class compounds.

Further, Oyler said the Beigene pipeline includes PD-1 and PD-L1 candidates and he expects both to be first-in-China. The PD-1 has best-in-class potential and will be in the clinic in the next two months according to Luo.

The pipeline also includes two monoclonal antibodies (undisclosed) and three small-molecule candidates (including indoleamine 2,3-dioxygenase [IDO] and interleukin-2-inducible kinase [ITK]).

In November 2014, Beigene raised $75 million in financing from Hillhouse Capital and CITIC PE as well as initial angel and strategic investors and unnamed American blue-chip investors. (See *BioWorld Today*, Nov. 19, 2014.) //

OTHER NEWS TO NOTE

Oncolytics Biotech Inc., of Calgary, Alberta, said the EMA granted orphan drug designation for lead candidate Reolysin for the treatment of pancreatic cancer. The EMA submission included survival data from the REO 017 study of the oncolytic virus-based drug in addition to gemcitabine in pancreatic cancer patients. In separate news, Oncolytics said it received a letter from the Nasdaq OMX Group determining that the company is eligible for an additional 180-calendar-day period, until Oct. 26, 2015, to regain compliance with the minimum $1 per share rule for continued listing.

Spark Therapeutics Inc., of Philadelphia, and **Clearside Biomedical Inc.**, of Alpharetta, Ga., said they entered an option agreement under which Spark acquired licensing rights to Clearside's microinjector technology to deliver gene therapies to the back of the eye. The companies will study the possibilities of using Clearside's microinjector technology to deliver viral vectors to the choroid and the retina through the suprachoroidal space. Clearside is currently in a phase II trial in macular edema associated with uveitis and a phase II trial in macular edema associated with retinal vein occlusion.

Thetis Pharmaceuticals LLC, of Southport, Conn., presented preclinical data at the GTC Diabetes Summit and Diabetes Drug Discovery & Development Conference in Boston, showing that oral candidate TP-113 has the potential to reduce insulin resistance, decrease hepatic glucose output, and reduce plasma triglycerides. TP-113 is a small molecule designed to deliver both metformin and DHA.

Sanbio

Continued from page 1

Exchange to help it advance SB623, its lead mesenchymal stem cell-based treatment for chronic stroke. The program, in joint development with Sumitomo Dainippon Pharma Co. Ltd., will enter phase IIb testing this year.

The company sold 4 million shares, 8.6 percent of its common stock, for ¥2,000 (US$16.80) per share, for gross proceeds of about ¥8 billion (US$67.2 million). Shares closed at ¥1,655 on Tuesday.

Founded by two friends in 2001 amid a cluster of small biotechs nestled near Berkeley, Calif.'s Takara Holdings Inc. sake factory, Sanbio moved first to Mountain View, Calif., and then this year to Tokyo, where it already had an office. It is led by co-CEOs Keita Mori and Toru Kawanishi.

Classmates in the University of Tokyo's masters program in biochemistry, the friends went their separate ways, with Mori taking a job with Kirin Brewery Ltd. and Kawanishi starting out at the Boston Consulting Group. But seven years later, with both looking for a new challenge, the friends got to talking about starting a biotech company that would have "a huge impact on society," Mori told *BioWorld Today*.

Seeing the genomics and proteomics fields already beginning to fill with potential competitors, they chose to focus on regenerative medicine, favoring the field in part because Japan had already established a technological advantage in the area. Sanbio, translated casually as "Mr. Bio," was born.

From the start, the company focused solely on allogeneic stem cell therapy, with scalability as a chief priority. Further optimizing for potential success, they sought to focus on the immuno-privileged area of brain regeneration. Though they worked with fetal-derived stem cells at first, the friends soon veered toward a new technology from Japan that enhanced the neuro-regenerative properties of adult-derived marrow stromal stem cells.

The Notch-transfection approach that the company eventually adopted for their lead candidate, SB623, helps form neuroprogenitor cells for the potential implant treatment of stroke & neurological diseases.

In February 2014, top-line clinical data on the SB623 made its first big showing at the International Stroke Conference. The open-label phase I/IIa study tested SB623 in 18-patients between six months and 16 months after stroke, people representative of the post-stroke rehabilitation population that generally lose momentum in their rehabilitation three to six months after their strokes.

Each were given three doses of the bone marrow-derived SB623 in the region adjacent to the damaged part of their brain. Patients showed statistically significant benefits on three separate measures of stroke at six, nine and 12 months after treatment.

As development has progressed, Sanbio has drawn substantial interest in the program. In February 2010, Tokyo-based Teijin Ltd. was the first partner to invest in its future. Making its first major move into the regenerative medicine market, Teijin took an equity stake of undisclosed size in the company and gained an exclusive licensing agreement to develop and sell SB623 in Japan, where stroke is the most prevalent cardiovascular disease, according to a review of epidemiology and registry studies published in the January 2013 edition of the *Journal of Stroke*.

Later in 2010, Sumitomo Dainippon, Japan's 13th largest drugmaker by market capitalization, took an option on SB623. After seeing the full results of the phase I/IIa testing, it exercised that option in September 2014, forming a joint development and license agreement with Sanbio, gaining exclusive marketing rights for the program in the U.S. and Canada.

Under terms of the agreement, Sumitomo Dainippon provided Sanbio $6 million up front, and committed to milestone payments of up to $74 million during the clinical development of the program. If launched, Sanbio would supply the finished product to Sumitomo Dainippon and receive double-digit percentage royalties based on sales as well as sales milestone payments if it hits certain sales goals, up to a total of $125 million. Expenses incurred in connection with the joint development will be shared equally between the two companies.

After the Sumitomo Dainippon deal, Mori said the SB623 is "very well funded" through phase III. "It gives us a very strong partner from the standpoint of development and marketing," he said. "It gives us stability to finance the product to launch, and good upside from the royalty payment of 17 percent and substantial revenue from manufacturing and product supply."

While Sanbio has not yet disclosed when its phase IIb trial of SB623 will read out, it has pledged to start the trial this year, as well as a separate phase II study of SB623 in traumatic brain injury, an indication it plans to partner after validating with additional data, said Mori.

Programs in retinal disease and Parkinson's disease earlier in Sanbio's pipeline have shown promise in animal studies, but will require further R&D, Mori said.

In addition to its own clinical progress, Mori said that the decision to take the company public turned in part on the changing regulatory landscape for regenerative medicine in Japan, where an expedited approval system for regenerative medicines went into effect in November. (See *BioWorld Today*, May 23, 2014.)

The new rules create a category of conditional approval and reimbursement which companies can seek on the basis of just phase I/II data confirming safety and indicating a product is likely to be effective.

"Review and approval will be much better facilitated," said Mori. Last year, the company, once headquartered in Mountain

See Sanbio, page 8

Kythera

Continued from page 1

known as submental fat.

In March the FDA's Dermatologic and Ophthalmic Drugs Advisory Committee voted unanimously to support the product's approval. The agency wasted no time in coming to a decision ahead of its planned PDUFA date of May 13.

According to the Westlake Village, Calif.-based company Kybella becomes a first-in-class submental contouring injectable drug, which is a patented formulation of a pure, non-animal derived version of deoxycholic acid, a naturally occurring molecule in the body that aids in the breakdown of dietary fat.

It has been the subject of 19 clinical studies involving more than 2,600 patients covering a span of ages (19-65) and BMI (18-40). The company said it submitted a new drug application (NDA) to the FDA in May last year with the safety and effectiveness based on positive and consistent results from two pivotal phase III trials, REFINE-1 and REFINE-2, which enrolled 1,022 adults. Participants were randomly assigned to receive Kybella or a placebo for up to six treatments. The results showed that reductions in submental fat were observed more frequently in participants who received Kybella vs. placebo and patients reported significant improvement in the visual and emotional impact of treatment.

In an FDA announcement it said that Kybella will be administered as an injection into the fat tissue in the submental area where patients could receive up to 50 injections in a single treatment, with up to six single treatments administered no less than one month apart.

The company has already filed regulatory applications in Canada, Switzerland and Australia. (See *BioWorld Today,* March 6, 2015.)

Although Kythera's shares (NASDAQ:KYTH) vaulted 25.3 percent when it announced the unanimous adcom vote in March, the approval of Kybella did not get investors excited with the company's shares trading Wednesday afternoon at $45.70, down about 4 percent. //

Sanbio

Continued from page 7

View and still running its R&D, manufacturing and operations largely from there, flipped its structure to site its official headquarters in Tokyo. "But having headquarters in Japan gives us a good opportunity in the near future to come to prosper as a global regenerative medicine company," said Mori. (See *BioWorld Today*, Dec. 3, 2014.) //

NSCLC

Continued from page 1

Clovis Oncology Inc.) or AZD9291 (mereletinib, Astrazeneca plc).

"Now there's a treatment option for patients who have failed current clinical EGFR agents," the Dana-Farber Cancer Institute's Pasi Jänne told *BioWorld Today*. Jänne is the lead author of the paper describing the AZD9291 trial results.

Ross Camidge from the University of Colorado, who is the senior author of the rociletinib paper but has treated patients with both drugs, said that "both are game-changers."

The drugs, both of which have received breakthrough designation from the FDA, could be the first options for patients who have developed resistance to EGFR inhibitors via the T790M mutation – a mutation that is responsible for resistance development in around 50 percent to 60 percent of patients treated with first-generation EGFR inhibitors such as Tarceva (erlotinib, Genentech/Roche AG, Iressa, (gefitinib, Astrazeneca plc) and Gilotrif (afatinib, Boehringer Ingelheim GmbH).

Clinical development of AZD9291 is "definitely further along than what is in the paper," Jänne said.

The drug is in other trials including the randomized phase III FLAURA study to compare it directly to Iressa and Tarceva as a first-line treatment for patients with EGFR mutations, in the hopes that initial treatment with a drug that is effective against T790M mutated tumors will delay the emergence of such mutations, beefing up what is the biggest drawback of targeted agents – their relatively short season of effectiveness.

Though the T790M mutation was first described 10 years ago, it took several failed attempts to develop effective inhibitors. AZD9291, however, has progressed rapidly in the clinic. Jänne said the first patient was dosed in March 2013, and Astrazeneca has said it plans to file for approval in the first half of this year.

Jänne and his colleagues enrolled 253 patients with locally advanced or metastatic non-small-cell lung cancer (NSCLC) with EGFR activating mutations. They found that the response rate among all patients was 51 percent. At 61 percent, the response rate was much higher in patients who had a T790M mutation. In patients where no such mutation could be detected the response rate was only 21 percent. Such patients benefited for a longer time as well, for 9.6 vs. 2.8 months.

In a separate study, 130 patients treated with rociletinib responded at a rate of 59 percent for T790M positive patients, and 29 percent if they did not have the mutation. In patients with the mutation, the drug kept working for a median 13.1 months, which was significantly longer than the 5.6 months seen in patients without the mutation.

Rociletinib, too, is in phase III trials, with the TIGER-3 trial comparing it to chemotherapy as second-line agent for patients with EGFR mutations. Phase II trials are testing it as first-line and second-line agent.

Though the AZD9291 trial is larger and there are some differences in side effect profiles – most notably, rociletinib came with a higher risk of hyperglycemia – an editorial accompanying the two papers stated that the two trials had "similar results" in terms of response rate and duration.

In the editorial, which was published along with the trial data in the April 30, 2015, issue of *The New England Journal of Medicine*, Ramaswamy Govindan of Washington University in St. Louis wrote that "finding EGFR T790M in tumor specimens after initial therapy with first-generation EGFR tyrosine kinase inhibitors now has practical relevance. In the immediate future, before the drugs are approved and widely available, these patients should be considered for ongoing clinical trials with T790M-specific EGFR tyrosine kinase inhibitors."

AZD9291 is also being tested in combination with the anti PD-1 antibody MEDI4736 (Astrazeneca).

Immunotherapies are currently in empire-building mode, being tested in a large number of tumor types in hopes of making their durable benefits a common outcome.

For now, though, Jänne pointed out, "it's the minority" of patients that responds to immuno-oncological approaches.

While those responses that occur are likely to be durable, it is only 10 percent to 15 percent of lung cancer patients who respond to immunotherapies at all. And there is not yet a way to predict whether a patient will be among the lucky responders.

For this reason, he said, for the time being if a patient has the right mutation for a targeted drug, "we start those patients with targeted therapy, because the track record is so much better to date."

Camidge said that the hope that eventually, all or most patients will benefit from immuno-oncology drugs is a sign that "there's a certain short-term amnesia going on," because that was at one point the assumption about EGFR inhibitors.

"We eventually had to figure out who they worked in, or who they worked best in," he said.

Likewise, "monotherapy with [immuno-oncology] is not a panacea. And for now, the types of tumors that immuno-oncology approach works best in – heavily mutated tumors with chaotic genomes – are in some ways the opposite of oncogene-driven tumors.

How the two approaches overlap "has to be explored," Camidge said. And in the meantime, in cases where tumors have restarted their growth after initially responding to the current generation of EGFR inhibitors, when the tumor responds to rociletinib or AZD9291, "it's a second miracle for those patients." //

Tyrogenex

Continued from page 1

a drug that could also be differentiated in the crowded AMD market by its dual action, inhibiting both VEGF and PDGF.

But it's likely the fact that X-82 offers a once-daily oral tablet alternative to monthly or every-two-month intravitreal injections required by market leaders Eylea (aflibercept, Regeneron Pharmaceuticals Inc.) and Lucentis (ranibizumab, Roche AG) that has patients flocking to clinical sites in the trial dubbed APEX (wet AMD in Previously treated Eylea patients with X-82).

"We have almost 20 sites active in the U.S. and [seeing] very quick enrollment," said Michael D. Webb, Tyrogenex president and CEO. "A lot of patients are really excited to have the opportunity to avoid these injections into the eye and switch to oral therapy.

"We think [X-82] could be something that really has the potential to revolutionize the space," he told *BioWorld Today*.

APEX is expected to enroll 132 subjects who had previously received treatment with Eylea and will measure as the primary endpoint the mean change in visual acuity score from day one to 52 weeks after randomization. X-82, a small-molecule tyrosine kinase inhibitor (TKI), will be administered daily, with patients in that group monitored to determine whether they need additional treatment by way of Eylea injections. Looking for a reduction in the number of those injections is another key endpoint needed for the duration of the study for X-82-treated patients vs. the control group receiving Eylea as directed.

There will be four groups, with one receiving a placebo pill and the others receiving various doses of X-82, Webb said. "Of course, what we're hoping is that patients receiving our compound have equal or improved vision vs. placebo and, hopefully, many fewer Eylea injections."

Tyrogenex is the only firm in the clinic with an oral wet AMD therapy designed to inhibit VEGF, or vascular endothelial growth factor, receptor, a target that has been firmly established in the wet AMD space thanks to the success of injectable anti-VEGF drugs Eylea and antibody therapy Lucentis. The VEGF receptor plays a key role the proliferation of endothelial cells for new blood vessels, which begin growing abnormally in patients with wet AMD.

But PDGF, or platelet-derived growth factor, has proved part of the problem, too. PDGF is linked to the regulation of pericytes that provide support for developing vessels. It's been shown that the new blood vessels, as part of the choroidal neovascularization that characterizes wet AMD, comprise both endothelial cells and pericytes, suggesting greater efficacy with a dual-action approach.

Combining inhibitors of both is the idea behind Ophthotech Inc.'s phase III studies for Fovista, an anti-PDGF therapy it is administering in combination with Lucentis (ranibizumab), the anti-VEGF therapy sold by Roche AG and Novartis AG. New York-based Ophthotech inked a deal with Novartis in 2014.

Ophthotech reported data from a 449-patient phase IIb study showing that Fovista plus an anti-VEGF agent demonstrated statistically significant superiority vs. Lucentis monotherapy, with patients in the combo group gaining a mean of 10.6 letters from baseline vs. 6.5 letters in the monotherapy group, representing a 62 percent comparative benefit from baseline.

Tarrytown, N.Y.-based Regeneron also is looking at a combination approach. In early 2014, it inked a deal with Bayer AG, of Leverkusen, Germany, to jointly develop an antibody against PGDF for use with Eylea. And Molecular Partners AG, which is developing late-stage anti-VEGF-A candidate abicipar in wet AMD in partnership with Allergan Inc. (recently acquired by Actavis plc), has a bispecific Darpin ((designed ankyrin repeat protein) molecule) binding to both VEGF-A and PDGF-B in preclinical development.

Tyrogenex's compound was specifically designed by scientific co-founder Chris Liang to have dual pathway targets, Webb said. "I think that can be quite advantageous. Certainly, both pathways are active in the disease."

Presenting at the Angiogenesis, Exudation and Degeneration 2015 meeting in Boston in February, investigator Jason S. Slakter reported phase I data showing that 22 of the 28 evaluable patients, who previously had been treated with injection therapy – gained nearly five letters on the eye chart. The open-label, ascending repeat-dose trial tested doses of X-82 ranging from 50 mg to 300 mg, examining patients' eyes every four weeks.

A MULTIBILLION MARKET

Tyrogenex hopes to have data from the APEX trial "within 36 months," Webb said. The firm expects to launch a financing effort this summer to raise sufficient funds for completing the study; beyond that, it has a number of options. "We're always actively in discussions with potential partners," he said.

The wet AMD market is big and getting bigger, with the baby boomers reaching advanced age. And following the success of Lucentis and Eylea, more drugs are filling pipelines. According to Cortellis Clinical Trials Intelligence, a total of 67 clinical studies are ongoing, with most drugs targeting VEGF or PDGF, and a range of administration from injections to implantable devices.

A few firms are working to develop topical eye drop formulations of drugs for wet AMD, but it remains to be seen whether those will succeed in replacing the intravitreal injections. Ohr Pharmaceutical Inc. is working on an eye drop product, OHR-102 (squalamine), expected to advance toward a phase III study despite mixed results from a phase II study reported earlier this year. But OHR-102, which is designed counteract multiple growth factors and pathways implicated in the angiogenic process, including VEGF, PDGF and basic fibroblast growth factor, is being tested in combination with an injectable anti-VEGF therapy. (See *BioWorld Today*, March 30, 2015.)

Still, the market is likely large enough for multiple players.

See Tyrogenex, page 12

Allicense

Continued from page 1

producing a scientific paper but rarely with a clinical milestone in mind.

But as VC dollars moved further downstream to programs already in human trials, funding from foundations and other not-for-profits became an indispensable source of early stage financing. That change wasn't lost on the funding organizations. Increasingly, they're applying the lens of business discipline rather than of charitable giving and seeking comprehensive partnerships with biotechs rather than one-shot gifts.

A panel at next week's Allicense 2015 conference will explore in greater detail the phenomenon of strategic partnering between biotechs and not-for-profits in a session alluding to return on investment from "unusual places."

When VCs stepped back, "a big hole" developed in early stage company formation, according to Chris Ehrlich, managing director of the advisory firm Locust Walk Partners and senior advisor to the Peter Michael Foundation (PMF), which aims to improve the diagnosis, treatment and management of prostate cancer.

"For a while, the strategic arms of pharmaceutical companies got involved and made some investments, but that's really not their job," Ehrlich told *BioWorld Today*.

Instead, foundations quickly spotted an opportunity to help accelerate promising therapies that fit within their research missions. For example, the PMF, established by the British technology entrepreneur, had a longstanding tradition of inviting donors to an annual dinner at the celebrated Northern California winery his family established and managed. But after many years of funding academic research that produced an ever higher stack of papers but no treatments, the PMF began to question the value of its donations.

"It wasn't a very efficient model," Ehrlich recalled. "When people give money, they want accountability."

Ehrlich worked with the PMF to establish Cancer Solutions LLC, which is operated under the jurisdiction and governance of the PMF, a 501(C)(3). However, Cancer Solutions allows high net worth individuals to invest in specific prostate cancer projects that have both scientific and commercial potential. Although the PMF remains committed to improving the diagnosis and treatment of prostate cancer, "by putting a commercial lens on the project, we believe we can make a greater impact further and faster and, in the process, provide the opportunity for an investor return, albeit not at historic venture capital levels," Ehrlich explained.

A second company, Prostate Management Diagnostics Inc. (PMDI), emerged from a collaboration between the PMF and the Genome Institute at Washington University School of Medicine, according to Doug Fisher, an executive in residence at Interwest Partners who serves as president of PMDI.

"This is a very unique concept," Fisher said. "For years, Peter Michael had given money away to academics who would publish their findings, but that didn't really change the practice of medicine for prostate cancer patients."

PMDI also is seeking to achieve that goal.

"We had an opportunity to leverage the resources of the Peter Michael Foundation to create a company along with Washington St. Louis," Fisher said, noting the medical school created a sponsored research agreement to cement the program in place. To date, the start-up, formed in October 2014, has raised approximately $1.2 million.

'THIS IS MORE THAN A SURFACE SCRATCHER'

The PMF isn't alone. The venerable Leukemia & Lymphoma Society (LLS), established 65 years ago, continues to look for new funding strategies despite surpassing $1 billion in funding across its history.

"Until seven years ago, the funding went exclusively to research projects in academic settings at research institutions all around the world," said Louis DeGennaro, president and CEO of the LLS. "At that time, we were deploying $50 million a year and funding a portfolio of 300 academic projects. When I looked at that portfolio, what I saw was that, every year, about 10 percent moved out of discovery into development. They were moving toward a therapy for patients, but they were floundering because you can't really develop drugs in an academic setting."

The LLS created the Therapy Acceleration Program to harvest promising projects from the grant program and accelerate their development with the goal of "getting them into the hands of biotech or pharma to deliver products to patients," DeGennaro told *BioWorld Today*. To date, two spinouts have emerged from the program and more are on the way.

The LLS also began to partner directly with biotechs, looking for companies with late preclinical assets that might have applications in lymphoma or leukemia but were insufficiently funded to advance into human studies. With 10 drug development professionals on its staff, all with advanced degrees in medicine or pharmacology, and with input from key opinion leaders around the world who serve as its medical advisors, the LLS was ideally equipped to vet potential assets.

So far, the organization has deployed from $1 million to $12 million for individual programs ranging from late preclinical or investigational new drug-enabling studies to pivotal trials.

"We don't have deep enough pockets to fully fund a drug development program," DeGennaro admitted. "We're in it for a short period of time, a couple of years. Our dollars are designed to help companies get over a particular development hurdle. Our hope is that, when they do that, they'll be able to go back to the capital markets and raise more money or they will get a big pharma partner."

To date, the LLS has been involved in five such projects that attracted major pharma deals.

Laura Shawver, founder and director of Cleave Biosciences and,

See Allicense, page 13

Tyrogenex

Continued from page 10

Current therapies alone total roughly $7 billion per year, Webb pointed out, acknowledging that "there's a lot of competition and a lot of opportunities, but we have the only oral therapy currently in active trials."

Tyrogenex also has plans to test X-82 in cancer. The drug is in two investigator-sponsored trials, which are "progressing quite well," he said. It's designed to have a high potency and a short half-life, with the theory that will improve the safety profile, and "to date, we've seen no dose-limiting toxicity. It has a much cleaner safety profile than other TKIs in the area," which opens up the possibility of combination treatment.

"Many times, the toxicity of multiple drugs overlapping makes that impossible," he added. "But X-82 in combination is quite tolerable. So we'll be pursuing [development] in solid tumors, but we haven't disclosed yet where we'll be going."

Tyrogenex, of Palm Beach Gardens, Fla., has about 10 full-time employees, with more than 15 contractors. It also has taken advantage of scientific founder Liang's connection with China – the medicinal chemist had been one of the top undergraduate students in China before pursuing a graduate degree in the U.S. at Princeton – as well as connections with colleagues at former company Sugen Inc., which developed approved cancer TKI Sutent (sunitinib malate), now owned by Pfizer Inc.

"Over the years, we've been able to leverage a lot of work in China in terms of preclinical and manufacturing," Webb said, which has allowed the firm to accomplish more substantial work than its modest size might suggest.

Tyrogenex was one of several companies formed out of Biocatalyst International Inc., a start-up incubator launched by Genzyme founder Sheridan Snyder. Both it and Xcovery LLC were formed around science developed by Liang, who serves as chief scientific officer for both companies. Webb, who came on board in March, also helms both firms.

"We have a common scientific legacy and many common investors, but we have separate compounds and separate IP," he explained.

The two firms raised money jointly until 2009, when they formally separated. Tyrogenex raised $15 million last year in a series D financing from Brace Pharma, the U.S. investment arm of EMS S/A, a large pharma headquartered in Brazil.

Last fall, Xcovery, which is developing small-molecule anaplastic lymphoma kinase (ALK) inhibitor X-396 in ALK-positive non-small-cell lung cancer patients, received commitments for a $20 million investment from Chinese firm Betta Pharmaceutical Co. (See *BioWorld Today*, Oct. 29, 2014.) //

IN THE CLINIC

Agios Pharmaceuticals Inc., of Cambridge, Mass., said it plans to advance into clinical development AG-881, a small molecule that has shown in preclinical studies to fully penetrate the blood-brain barrier and inhibit isocitrate dehydrogenase-1 (IDH1) and IDH2 mutant cancer models, in collaboration with its cancer metabolism partner **Celgene Corp.**, of Summit, N.J. AG-881 will be the third IDH mutant inhibitor discovered by Agios to enter clinical development.

Arena Pharmaceuticals Inc., of San Diego, disclosed favorable results from a phase I single-ascending dose trial of APD371, described as a highly selective and potent agonist of the cannabinoid 2 (CB2) receptor currently in development for the treatment of pain and potentially fibrotic diseases. The randomized, double-blind and placebo-controlled trial enrolled 56 healthy adults to evaluate the safety, tolerability and pharmacokinetics of single-ascending doses of APD371. Dose responsive exposure was observed over the explored dose range of 10-400 mg with good tolerability at all doses administered, Arena said.

Ascendis Pharma A/S, of Copenhagen, Denmark, said its phase I single-ascending dose study of Transcon Treprostinil produced dose-dependent increases in plasma treprostinil levels in line with expectations. However, treprostinil-related injection-site tolerability issues did not meet the criteria defined in the target product profile. Ascendis now intends to conduct additional research on new product formulations and plans to resume clinical development when product improvements to mitigate current limitations have been addressed.

Benitec Biopharma Ltd., of Sydney, reported that investigators have dosed the fifth patient in the company's safety-focused phase I/IIa dose escalation trial of TT-034 for hepatitis C virus infection. The patient was the last enrolled in the trial's second cohort. Benitec is now screening patients for inclusion in the third cohort in anticipation of a review from the study's data safety monitoring board that would allow the trial to proceed.

Celsion Corp., of Lawrenceville, N.J., said it plans to expand its ovarian cancer development program, expected to begin in the second half of this year, to include a phase I dose escalating trial evaluating the DNA-based immunotherapy GEN-1 in combination with Avastin (bevacizumab, Genentech Inc./Roche AG) and Doxil (doxorubicin) in platinum-resistant ovarian cancer patients. The company confirmed that it intends to start a phase Ib dose escalation trial in newly diagnosed ovarian cancer patients in the third quarter of this year. (See *BioWorld Today*, Feb. 23, 2015.)

Allicense

Continued from page 11

prior to that, the Clearity Foundation, said the mission of not-for-profits continues to change and grow alongside that of the biotech industry. Clearity was initially formed to improve the outcomes of women with ovarian cancer by helping them, for starters, to gain access to tumor profiling, but that process "is starting to become a commodity," Shawver said.

The next step for the foundation is to operationalize treatment by marshaling its database and helping to improve the collection of follow-up data – still a major issue for ovarian cancer and, indeed, oncology treatment, in general.

Shawver's interest in interacting with biotechs and medical professionals is to improve the efficiency and effectiveness of clinical trials – a process that also would save money for biotechs and, potentially, prolong and improve the lives of more patients.

"We, as an oncology community – oncologists and scientists and drug developers – need to find a way to help people get on clinical trials earlier who potentially match to an alteration because they may have a better chance to respond," she said. "We have to shift the paradigm for how we think about clinical trials. We have to place people in trials that make sense for them, wherever those trials happen to be running. Ultimately, insurance companies then will be reimbursing drugs that work instead of reimbursing drugs that don't work."

Medical not-for-profits and patient advocacy foundations aren't blind to the risks inherent in helping to bankroll early stage companies, said Mark Fischer-Colbrie, a board member of the Juvenile Diabetes Research Foundation (JDRF), which is the single largest funding source for diabetes research. But in addition to funding, they also offer an array of resources that can help young biotechs to lower their business risks.

"Given our network of contacts, we can ask an expert from anywhere in the world to talk with a small company that's looking to move an asset forward," Fischer-Colbrie pointed out. That advice might range from clinical trial design to regulatory strategy to an appropriate reimbursement structure.

JDRF also keeps an eye on the global diabetes landscape to identify technology gaps and tries to plug those by supporting compelling drug candidates and technologies. Currently, the foundation is funding nearly four dozen clinical trials.

"We're highly proactive," Fischer-Colbrie said. "We know there are some gaps that will not be filled unless JDRF steps in, whether that involves moving something from an academic setting to an early stage drug discovery company or seeking to persuade a biopharma company to redirect or expand research with a promising therapeutic into type 1 diabetes."

With deep interest and resources in a given therapeutic space, applying a business lens to the grant-making process is a natural follow on.

"We're still learning," Fisher conceded. "This is an experiment, and we'll see if it works. But we know already that we can leverage a built-in base of investors who support the foundation as well as the connections the foundation has with researchers and industry. That's an incredible value-add."

An underlying theme of this year's Allicense conference is a focus on shaking up traditional models of biotech financing and partnering and exploring new options. In Ehrlich's view, the new paradigm of foundation funding for scientific research and biotech discovery fits squarely into that mold.

"This is more than a surface scratcher," Ehrlich maintained. "Science continues to advance. Venture capital backed away early because it was a poor economic model relative to limited partners. Pharma wasn't really the right group to get involved early because they like to bring things in when they're better cooked. This is a cool model to move the science to a point where it's de-risked and people will be more interested." //

IN THE CLINIC

Cytrx Corp., of Los Angeles, said a case study of a 54-year-old male patient with recurrent left parietal lobe glioblastoma multiforme (GBM) has been published online in the *Journal of Nuclear Medicine & Radiation Therapy*. The patient had completed treatment with radiation and temozolomide more than two years prior to being enrolled onto the phase II GBM aldoxorubicin trial, and no other treatment for his malignancy was administered in the interim. A prior debulking procedure had demonstrated progressive tumor growth. While on the aldoxorubicin trial, the patient received a single cycle of intravenous aldoxorubicin 350 mg/m2 (260 mg/m2 doxorubicin equivalents). According to both clinical and radiological assessments (MRI brain scans) performed four and six weeks after aldoxorubicin therapy, the patient appeared to experience tumor progression. However, histopathological assessment of the tissue following a subsequent tumor debulking procedure showed no evidence of recurrent glioblastoma throughout the entire surgical specimen. Investigators believe that the presence of tumor seen in the MRI scans post-aldoxorubicin treatment likely represents pseudo-progression, commonly seen in CNS malignancies undergoing radiation therapy, and may reflect aldoxorubicin's ability to allow doxorubicin to enter the brain tumor and induce tumor necrosis.

Replicor Inc., of New York, reported on a study examining the safety and efficacy of REP 2139-Ca monotherapy, followed by combined therapy with Pegasys (pegylated interferon alfa-2a, Roche AG) in Caucasian patients with chronic hepatitis B / hepatitis D co-infection. Interim data, primarily from the REP 2139-Ca monotherapy phase of the trial, demonstrated that REP 2139-Ca was well tolerated and resulted in the rapid and simultaneous multi-log reduction of both serum HBsAg and HDV RNA, the company said. Replicor also said that many patients had no detectable serum HBsAg or HDV RNA after 15 weeks, before entering the combination therapy phase of the trial. The data were presented at the 2015 European Association for the Study of the Liver meeting in Vienna.

IN THE CLINIC

Xbiotech Inc. has enrolled the first patient in its revised phase III study of Xilonix in metastatic colorectal cancer patients. The study initially launched in March 2013 and patients were recruited at more than 60 U.S. cancer centers. But Xilonix paused the study to propose changes in inclusion criteria to allow broader eligibility for cancer patient enrollment. The newly approved protocol enables recruitment of advanced, refractory colorectal cancer patients that includes those who have failed all standard therapies, the company said. The trial resumption arrives a little more than a month after the company joined Nasdaq with an IPO. (See *BioWorld Today*, April 16, 2015.)

PHARMA: OTHER NEWS TO NOTE

Astrazeneca plc, of London, said the FDA accepted the supplemental new drug application (sNDA) and granted priority review for Brilinta (ticagrelor) to treat patients with a history of heart attack. The sNDA is based on the results from the PEGASUS-TIMI 54 study, an outcomes trial enrolled more than 21,000 patients to investigate ticagrelor tablets plus low-dose aspirin, compared to placebo plus low-dose aspirin, for chronic secondary prevention of atherothrombotic events in patients who experienced a heart attack one to three years prior to study enrollment. Brilinta is approved to reduce the rate of thrombotic cardiovascular events in patients with acute coronary syndrome.

Perrigo Co. plc, of Dublin, has rejected the revised unsolicited offer from **Mylan NV**, of Potters Bar, UK, to acquire all of the outstanding shares of Perrigo for $75 per share in cash and 2.3 Mylan ordinary shares for each ordinary Perrigo share. The board previously concluded that Mylan's unsolicited proposal of April 8 of $205 per share significantly undervalued the company. Wednesday's announcement from Mylan continues to propose a price lower than the previously rejected proposal. Based on Mylan's unaffected price of $55.31 per share on March 10, 2015, the last day of trading prior to widespread public speculation that **Teva Pharmaceutical Industries Ltd.**, of Jerusalem, was considering an offer for Mylan, the value of the revised offer is $202.20 per Perrigo share. On April 21 Teva made a $40.1 billion bid for the generics heavyweight, valuing it at $82 per share in a half cash, half stock offer. (See *BioWorld Today*, April 9, 2015, and April 22, 2015.)

Takeda Pharmaceutical Co. Ltd., of Osaka, Japan, and its wholly owned subsidiary, Takeda Pharmaceuticals USA, of Deerfield, Ill., said they reached an agreement to resolve most of the Actos (pioglitazone HCl) product liability lawsuits pending in the U.S. Takeda will take a $2.7 billion charge against earnings in the fourth quarter of fiscal 2014 to cover the settlement and the costs associated with defending remaining cases and for other related litigation. The settlement will become effective if 95 percent of current litigants and claimants opt in, and Takeda will pay $2.37 billion into a settlement fund, rising to $2.4 billion if 97 percent or more of current litigants and claimants opt in. Takeda said it believes claims in the litigation are without merit and did not admit liability. The company said it is committed to making Actos available as a treatment option to improve glucose control in adults with type 2 diabetes in the 95 countries where it is approved, including the U.S. and Japan.

CLEARLY **CORTELLIS**

CORTELLIS COMPETITIVE INTELLIGENCE

Focused insight into the pharma competitive landscape.

Spot new drug opportunities and identify niche markets faster than anyone else with Cortellis™ Competitive Intelligence.

Covering more than 50,000 drug records. Enriched with pipeline analysis, daily conference reports, sales forecasts, patents, literature and more.

Explore Cortellis Competitive Intelligence – the most powerful single source of information for pipeline analysis.

When you want clarity—fast: Thomson Reuters Cortellis.

THOMSON REUTERS™