WEEK OF AUGUST 15, 2011

BioCentury

THE BERNSTEIN REPORT ON BIOBUSINESS

Volume 19 • Number 34 • Page A1 of 21

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Rebalancing act

BioCentury This Week

Cover Story

Rebalancing Act — The market turmoil saw investors scorch biotechs with product launches or weak balance sheets, but some specialists exploited the opportunity to clean up portfolios and go shopping for value plays.

Strategy

New Vision — After failing to capitalize on the approval of its first drug followed by a shareholder revolt, InSite has raised money to refocus on four ophthalmology programs it thinks can be moved through the clinic quickly./*A5*

Product Discovery & Development

Powering Down Cancer — The first data are beginning to emerge from a cluster of companies targeting the energy needs of malignant cells, based on a better understanding of why cancer cells use altered metabolic pathways./*A6*

Locking in Lebrikizumab — In the race to treat asthma with anti-IL-13 molecules, Genentech now has positive Phase II data and a biomarker for responders to lebrikizumab. Next up are data from MedImmune's tralokinumab./*A11*

Daclizumab in MS — The first look at the Select data for daclizumab from Biogen Idec and Abbott, and how the once-monthly subcutaneous approach compares to the marketed and Phase III competition./*A13*

Emerging Company Profile

Cancer Stem Cell Engine — Verastem believes it can produce an almost unlimited number of stem-like cells to use as screens for small molecules against CSCs./*A15*

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Ebb & Flow — Flurry for Forest finale. Pulmatrix has CALM investors. Vaxxas patches up nicely. Also: BMO; Adventrx; Affymax; Amylin; Arena; MannKind; Pharmasset, et al./*A16*

BioCentury 100™ Indicators

Week ended 8/12/11

PRICES	VOLUME
2130.98	1154.9M shrs
up 1%	up 3%

By Stacy Lawrence
Senior Writer

Companies in the midst of launching products or with weak balance sheets have been sold off or avoided by most investors during the market roller-coaster of the past two weeks. However, a handful of companies have been insulated from the carnage — their common threads being strong sales, pending or potential acquisitions, or positive data. Large caps as a group also held up relatively well.

In the last two weeks, the NASDAQ Biotechnology Index (NBI) fell 13%. The BioCentury 100 was off 12%, while the NYSE Arca Biotechnology Index (BTK) lost 17%. Over the same time, the S&P 500 and the NASDAQ were both off 9%, while the Dow Jones Industrial Average shed 7% *(see "Seeing Red," A2)*.

A sliver of good news emerged on Thursday and Friday last week — the NBI, BC100 and BTK each gained 6% over the two days — as biotechnology buysiders started shopping for discounts on companies with strong fundamentals and balance sheets.

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This Week in *SciBX*

Bromodomain Brake on AML — Tensha Therapeutics hopes to bring a bromodomain inhibitor into Phase I trials after a Cold Spring Harbor-led team used the strategy to treat AML in mice. Please see Table of Contents on A11.

BioPharm America Soon

Pre-conference partnering has started. Please see announcement following A21.

This Week on BioCentury TV

America's Health Advisor — IOM gets the hard questions. Please see Program Notes on A3.

www.biocenturytv.com

NewsMakers Expands

More names are added to the presenting company roster at the 18th Annual NewsMakers in the Biotech Industry conference. Please see announcement following A21.

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Lumps on launch

Almost every buysider contacted by BioCentury noted the punishment of companies with recent or upcoming launches.

The start of the market slide coincided with scaled down expectations for **Dendreon Corp.**'s Provenge prostate cancer vaccine following the company's 2Q call, which investors have taken as a bad indicator for biotech launches *(see BioCentury, Aug. 8)*.

Indeed, Dendreon was the worst performer among biotechs valued above $5 billion. The stock shed $26.53 (72%) to $10.37 in the past two weeks.

"Obviously the product launch stories suffered the most post-Dendreon," summed up David Chan of Jennison Associates.

Even **Vertex Pharmaceuticals Inc.** was off $7.37 (14%) to $44.49 in the same period, despite a positive launch for HCV drug Incivek telaprevir.

Vertex reported $74.5 million in 2Q sales of Incivek, half from stocking and half from end user sales. The numbers beat analyst estimates for end user sales, which were $31-$35 million.

Upcoming and ongoing launch stories also had the poorest showings in the $1-$4.9 billion segment. Among the top decliners is **Savient Pharmaceuticals Inc.**, which launched gout drug Krystexxa pegloticase in December. The stock was down $2.72 (39%) to $4.28 in the last two weeks after revenues missed consensus estimates.

Other big drops in the $1-$4.9 billion market cap band were **InterMune Inc.**, which was off $10.44 (31%) to $22.94, and **Human Genome Sciences Inc.**, which shed $5.33 (25%) to $15.68.

"Any company with high-priced drugs and a phenotype like Dendreon has been hit. Investors are now very concerned that launches are even more risky than before," said Kurt von Emster of venBio. "InterMune will have a high-priced drug launching in Europe soon. Human Genome Sciences continues to be under pressure, although they have done a good job tempering investor expectations about their launch."

InterMune plans to launch Esbriet pirfenidone in Europe in September to treat idiopathic pulmonary fibrosis. In March, HGS and partner **GlaxoSmithKline plc** launched lupus drug Benlysta belimumab in the U.S. Human Genome reported $7.8 million in 2Q sales, its first full quarter. The consensus estimate was $8.5 million.

One biotech mutual fund manager who asked to remain anonymous also cited Human Genome and InterMune, adding **Seattle Genetics Inc.** to the list as well.

Seattle Genetics dropped $3.10 (17%) to $13.93 in the last two weeks. The company has an Aug. 30 PDUFA for Adcetris brentuximab vedotin to treat Hodgkin's lymphoma and systemic anaplastic large cell lymphoma. In July, FDA's Oncologic Drugs Advisory Committee recommended accelerated approval.

Joep Muijrers of LSP is actually buying into some launch stories now.

"Following Dendreon's setback, which we believe came at the worst possible time in light of prevailing market conditions, it seems as if people are now questioning the entire therapeutic biotech model. We do not mind being on the other side of that bet," he said.

Bad clinical and regulatory news was responsible for the worst performances in three market cap segments under $1 billion.

In the $500-$999 million group, **Active Biotech AB**'s oral laquinimod missed the primary endpoint in a Phase III trial to treat relapsing-remitting multiple sclerosis (RRMS). The results were announced on Aug. 1, and Active Biotech was down SEK45.15 (57%) to SEK33.60 in the last two weeks. The compound is partnered with **Teva Pharmaceutical Industries Ltd.**, which fell $6.94 (15%) to $39.70 during the period.

In the $200-$499 million segment, **Insmed Inc.**'s Arikace to treat *Pseudomonas aeruginosa* infection in patients with cystic fibrosis (CF) was placed on clinical hold by FDA on Aug. 2. The stock was down $7.04 (61%) to $4.45 over the past two weeks.

Adventrx Pharmaceuticals Inc. was the worst performer in the last two weeks among the biotechs valued under $200 million. It was down $1.89 (64%) to $1.06 on last week's complete response letter for Exelbine vinorelbine injectable emulsion to treat non-small cell lung cancer (NSCLC). FDA said the company's trial needs to be repeated to verify the authenticity of the drug product used *(see B9)*.

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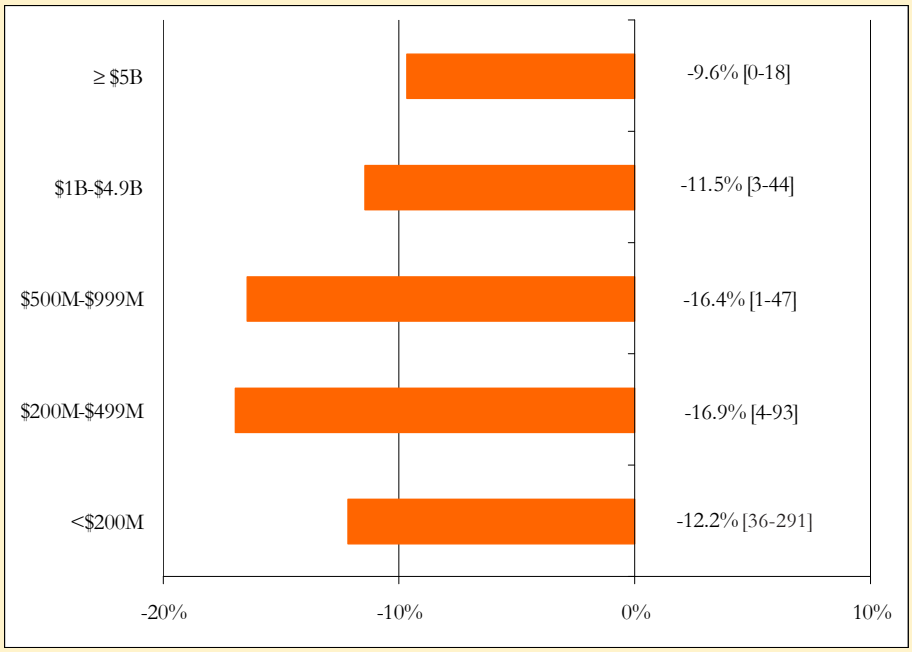
Seeing red

For the past two weeks, biotechs across the board have been battered even more than the overall markets. Companies in the small to mid-cap ranges sustained the most damage, dropping more than 16%.

The BioCentury 100 was down 12% for the past two weeks while the Dow and S&P 500 fell 7% and 9%, respectively. The Amex Pharmacuetical Index shed 7.4%

Companies are grouped into market cap tiers as of July 29. Median percentage changes calculated for each market cap segment from July 29 through Aug. 12. Advancers-decliners are in brackets.



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On the heels of recent IPOs, genomics companies **Pacific Biosciences of California Inc.** and **Complete Genomics Inc.** were off on weak 2Q earnings. Pacific Biosciences dropped $5.05 (46%) to $5.96, while Complete Genomics lost $3.77 (30%) to $8.62.

Finding shelter

A handful of biotechs have weathered the market crash. **Cephalon Inc.** held its ground among companies valued above $5 billion, because its stock is underpinned by the company's pending acquisition by Teva for $81.50 per share, or $6.8 billion in cash.

The deal is expected to close this quarter. Even then, Cephalon finished the two weeks off $0.14 to $79.88.

AMAG Pharmaceuticals Inc. also had its shares backstopped by a potential deal. Last week, it rejected an $18 per share cash bid ($380.9 million) from MSMB Capital Management. The company says it still plans to merge in a stock deal with cancer company **Allos Therapeutics Inc.** (NASDAQ:ALTH). AMAG added $0.16 to $14.97 over the two weeks.

"With some of the oncology and neurology names down since May, we are now buying them back, in some cases fairly aggressively."

Kurt von Emster, venBio

Luminex Corp. and **Genmab A/S** were the top performers in the $500-$999 million and $200-$499 million groups, respectively, over the last two weeks.

Strong 2Q earnings pushed Luminex up $1.69 to $22.04, while Genmab added DKK2.22 to DKK42.44 in the past two weeks, helped by positive Phase II data for ofatumumab to treat lymphoma.

von Emster noted that companies with strong sales "have held up reasonably well, including Jazz and Questcor."

Specialty pharma **Jazz Pharmaceuticals Inc.** was only off $0.61 to $39.86 in the last two weeks, while neurology and autoimmune play **Questcor Pharmaceuticals Inc.** added $0.51 to $31.56. Both are profitable.

The biotech mutual fund manager also cited **Pharmasset Inc.**, which gained $3.65 to $125.03 after a 2-for-1 stock split within the last two weeks. Investors remain enthusiastic about its oral HCV program. In contrast, competitor **Idenix Pharmaceuticals Inc.** fell $2.52 (38%) to $3.16.

Biotech cycles

Many biotech buysiders are using the market's gyrations to rotate within the sector, but say they won't pull the trigger on a stock purchase unless the company has a strong cash position.

Selena Chaisson of Bailard said she took some profits in June and became more defensive. During the downturn, she's been "selling names that were less impacted to buy names that were more impacted but in which we have high conviction." Chaisson declined to give specific names.

She added that she's also buying companies "where we have liked the technology but not the valuation until now."

As a small cap biotech specialist, she underscored the importance of a strong balance sheet given the lack of fundraising visibility. "We were careful all year to buy names that were well capitalized, and with the financing window now officially closed, we have become even more selective," she said.

von Emster said his buying has been focused on "very select names hit hard but with cash to last 18-24 months and catalysts in the next nine months." He said his firm's buying became more aggressive on Wednesday and Thursday.

In some ways, the selloff couldn't have come at a better time for venBio.

"We took some profits going into the summer, as there is traditionally a selloff after ASCO. We were about to do some small cap buying when the market sold off in late July," von Emster said. "With some of the oncology and neurology names down since May, we are now buying them back, in some cases fairly aggressively, and have removed much of our ETF hedge."

With a new publicly listed fund that started off in April with about €39 million ($56.9 million), and the potential to raise more, LSP's Muijrers is primarily focused on building positions. He's buying "well-run companies with strong balance sheets and potential blockbusters in development or even close to launch or already on the market that are trading at a significant discount as compared to only a few weeks ago."

Muijrers added: "Nobody knows where

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this all will end, but we are picking up shares of those companies that we feel are dragged down for no other reason than prevailing market sentiment."

That does not mean Muijrers is holding onto everything. "Clearly, we are also looking at capitalizing on gains from earlier in the year for a number of our positions where we feel that is appropriate," he said, "but we try to stay away from participating in any panic sales."

The biotech mutual fund manager who did not want to be named said he's been very active, increasing holdings of discounted stocks he likes and rotating holdings into names that were previously too expensive.

"In accounts where cash positions were high, we have been increasing net exposure. In accounts that were fully invested, we have been swapping positions to remain fully invested," he said.

The fund manager said his share sales have fallen into three categories: stocks that held up well, often with strong fundamentals, that were difficult to part with but were relatively expensive; stocks of companies with weak or deteriorating fundamentals that were sold to improve the quality of the portfolios; and large caps that were sold to make room for more small caps.

On the buyside, his purchases also have been of three main types: launch stories where the firm thinks the fundamentals are good but the stocks have suffered steep declines; microcaps that suffered disproportionate declines due to poor liquidity; and companies that had positive momentum and are now more reasonably valued.

> ***"Nobody knows where this all will end, but we are picking up shares of those companies that we feel are dragged down for no other reason than prevailing market sentiment."***
>
> **Joep Muijrers, LSP**

COMPANIES AND INSTITUTIONS MENTIONED

Active Biotech AB (SSE:ACTI), Lund, Sweden
Adventrx Pharmaceuticals Inc. (NYSE-A:ANX), San Diego, Calif.
Allos Therapeutics Inc. (NASDAQ:ALTH), Westminster, Colo.
AMAG Pharmaceuticals Inc. (NASDAQ:AMAG), Lexington, Mass.
Cephalon Inc. (NASDAQ:CEPH), Frazer, Pa.
Complete Genomics Inc. (NASDAQ:GNOM), Mountain View, Calif.
Dendreon Corp. (NASDAQ:DNDN), Seattle, Wash.
Genmab A/S (CSE:GEN), Copenhagen, Denmark
GlaxoSmithKline plc (LSE:GSK; NYSE:GSK), London, U.K.
Human Genome Sciences Inc. (NASDAQ:HGSI), Rockville, Md.
Idenix Pharmaceuticals Inc. (NASDAQ:IDIX), Cambridge, Mass.
Insmed Inc. (NASDAQ:INSM), Monmouth Junction, N.J.
InterMune Inc. (NASDAQ:ITMN), Brisbane, Calif.
Jazz Pharmaceuticals Inc. (NASDAQ:JAZZ), Palo Alto, Calif.
Luminex Corp. (NASDAQ:LMNX), Austin, Texas
Pacific Biosciences of California Inc. (NASDAQ:PACB), Menlo Park, Calif.
Pharmasset Inc. (NASDAQ:VRUS), Princeton, N.J.
Questcor Pharmaceuticals Inc. (NASDAQ:QCOR), Union City, Calif.
Savient Pharmaceuticals Inc. (NASDAQ:SVNT), East Brunswick, N.J.
Seattle Genetics Inc. (NASDAQ:SGEN), Bothell, Wash.
Teva Pharmaceutical Industries Ltd. (NASDAQ:TEVA), Petah Tikva, Israel
Vertex Pharmaceuticals Inc. (NASDAQ:VRTX), Cambridge, Mass.

BioCentury Company Index
August 15, 2011

Strategy

InSite's new vision

By Michael Flanagan
Senior Writer

InSite Vision Inc. thought it was poised for success in 2007 when, after 20 years of effort and more than $52 million raised from investors, the company's first drug, AzaSite 1% azithromycin ophthalmic solution, was approved by FDA for bacterial conjunctivitis (pink eye).

Instead, according to CEO Timothy Ruane, an ill-considered partnership and poor commercial planning got the company into trouble.

Insite now has re-emerged as a leaner entity. The company tapped the equity markets last month to fund its new plans to refocus on four clinical ophthalmology programs.

Ironically, Ruane said it was AzaSite that led to trouble, when the company licensed exclusive U.S. and Canadian marketing rights to Inspire Pharmaceuticals Inc. in 2007.

"InSite partnered with somebody who aspired to be a commercial ophthalmic organization," he noted. "It might have been smarter to take lesser terms with a partner that already was a commercial ophthalmic organization."

> ***"It might have been smarter to take lesser terms with a partner that already was a commercial ophthalmic organization."***
>
> **Timothy Ruane, InSite Vision**

AzaSite sales were sluggish after it was launched, in part because "the original marketing strategy involved selling it to ophthalmic specialists. But everybody knows that if your kid gets pink eye you take them to a GP," Ruane said.

Because of the slow sales, InSite needed money and ended up raising $60 million in a non-convertible note deal in February 2008 secured by the AzaSite royalties. But it had to offer investors a 16% interest rate to get it done *(see BioCentury, March 3, 2008)*.

According to Ruane, exasperated shareholders responded by waging a proxy battle that resulted in the removal of InSite's board and previous CEO in 2H08, and led the company to go into hibernation for all of 2009 and most of 2010.

InSite re-emerged late last year with a new management team, a 15-person staff — down from 80 prior to the AzaSite letdown — and a plan to refocus on its pipeline of ophthalmology products formulated using the company's DuraSite delivery system.

Ruane believes InSite can take advantage of the short duration and relatively inexpensive studies in the ophthalmic space "to get more drugs approved in the next two to four years than the company got across the finish line" in its previous two decades, he said.

"In lymphoma, it would cost $80-$85 million to conduct a Phase III trial with a four- or five-year survival endpoint," he said. In contrast, InSite expects to pay less than $8 million to conduct its next Phase III trial, which will begin this quarter and read out around YE12.

InSite chose an unusual protocol for the study, which is designed to obtain data to support approval of two separate investigational products to treat moderate to severe blepharitis. Both products, AzaSite Plus azithromycin/dexamethasone and DexaSite dexamethasone, use DuraSite.

The trial will compare AzaSite Plus vs. AzaSite and a vehicle solution, while simultaneously comparing DexaSite vs. a vehicle solution. The marketed version of AzaSite also will be compared vs. the vehicle solution.

InSite has an SPA from FDA for the study.

By year end, the company also plans to start a Phase III trial of ISV-303, a 0.075% ophthalmic solution of the NSAID bromfenac, to treat post-cataract inflammation and pain.

A planned Phase I/II trial of ISV-101, a 0.01-0.04% formulation of bromfenac for dry eye disease, will be up and running this year.

Ruane is hoping for results from the three trials by YE12. He added the company will consider marketing some or all of the products on its own.

InSite plans to lean on CROs to conduct its planned studies, he said, which should keep the company's annual burn rate at roughly $8 million.

To finance its plans, the company raised $22.2 million in July in a private placement of 37 million units at $0.60. Each unit consists of a share and a five-year warrant to purchase 0.4 shares. Each whole warrant is exercisable at $0.75.

Investors included members of InSite's management and board. Piper Jaffray acted as placement agent.

The company booked $11.2 million in royalities in 2010 and reported $2.9 million in royalties in the quarter ended March 31, 2011.

Meanwhile, **Merck and Co. Inc.** acquired Inspire earlier this year for about $430 million.

In addition to AzaSite royalties from Merck, InSite receives single-digit royalties on Besivance, a besifloxacin 0.06% ophthalmic suspension that uses DuraSite. **Bausch + Lomb Inc.** and **Pfizer Inc.** co-promote Besivance in the U.S. to treat bacterial conjunctivitis.

COMPANIES AND INSTITUTIONS MENTIONED

Bausch + Lomb Inc., Rochester, N.Y.
InSite Vision Inc. (OTCBB:INSV), Alameda, Calif.
Merck & Co. Inc. (NYSE:MRK), Whitehouse Station, N.J.
Pfizer Inc. (NYSE:PFE), New York, N.Y.

Product Discovery & Development

Powering down cancer

By Stephen Hansen
Senior Writer

The cancer metabolism field has been heating up over the last five years, and now is beginning to produce some of the first data for compounds aimed at stunting aerobic glycolysis, the energy-generating process that many tumor cells use to fuel their growth.

There are three cancer metabolism programs in the clinic, with more around the corner. The strategies companies are pursuing can broadly be placed into three buckets: preventing the production of cellular intermediates, limiting the energy available for DNA damage repair and using the byproducts of energy metabolism against the cancer cell.

Players employing the first approach include **Cornerstone Pharmaceuticals Inc.**, **Dynamix Pharmaceuticals Ltd.**, **Agios Pharmaceuticals Inc.** and **Ruga Corp.**, which are working on compounds that disrupt the cancer cell's biosynthetic machinery that produces the biomass necessary for proliferation.

In the second bucket, **Myrexis Inc.** and others are stunting DNA repair in tumors by limiting the energy available to the cell.

Finally, the technology transfer arm of **Cancer Research UK** and **AstraZeneca plc** are using the byproducts of glycolysis to destroy the cancer cell.

Companies also are identifying biomarkers that can stratify patients whose tumors are heavily reliant on these pathways or show when the pathways are working overtime.

AstraZeneca and Cancer Research Technology Ltd. (CRT) plan to enter the clinic by year end, while at least another two programs should begin Phase I testing in 2012 *(see "Cancer Metabolism Pipeline")*.

Shots in the dark

In normal cells, the primary metabolic goal is to generate energy in the form of ATP. In the presence of oxygen, energy production is based on the metabolism of glucose into carbon dioxide by oxidation of pyruvate in the mitochondrial tricarboxylic acid (TCA) cycle. This highly efficient mitochondrial oxidative phosphorylation pathway maximizes the amount of ATP generated from a molecule of glucose and can generate up to 36 ATP molecules per glucose molecule.

In anaerobic conditions, normal cells use glycolysis to convert glucose to lactate. It is far less efficient, producing only two

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Cancer metabolism pipeline

Selected compounds in development targeting cancer metabolism processes. (A) Being acquired by **Teva Pharmaceutical Industries Ltd.** (NASDAQ:TEVA); (B) Cephalon, which obtained GMX1777 in its acquisition of Gemin X Pharmaceuticals Inc., said the program is under evaluation; *Source: BCIQ: BioCentury Online Intelligencce*

Company	Product	Product description	Indication	Status
Polaris Pharmaceuticals Inc.	ADI-PEG 20	Pegylated arginine deiminase	Hepatocellular carcinoma (HCC)	Ph III
TopoTarget A/S (CSE:TOPO)/ **Astellas Pharma Inc.** (Tokyo:4503)	APO866	Nicotinamide phosphoribosyl transferase (NamPRT) inhibitor	Cutaneous T cell lymphoma (CTCL)	Ph II
Cornerstone Pharmaceuticals Inc.	CPI-613	Analog of alpha-lipoic acid that targets the mitochondrial enzymes pyruvate dehydrogenase (PDH) and alpha-ketoglutarate dehydrogenase	Hematological malignancies; solid tumors	Ph I/II
AstraZeneca plc (LSE:AZN; NYSE:AZN)/**Cancer Research UK**	AZD-3965	Monocarboxylate transporter 1 (MCT1) inhibitor	Cancer	Ph I/IIa to start 2011
Cephalon Inc. (NASDAQ:CEPH) (A)	Teglarinad (GMX1777)	NamPRT inhibitor	Metastatic melanoma	Ph I/II halted (B)
Dynamix Pharmaceuticals Ltd.	PKM2 program (DNX-03000)	Fructose biphosphate mimetic that binds pyruvate kinase M2 isozyme (PKM2)	Cancer	Preclin; start Ph I in 2012
Agios Pharmaceuticals Inc.	IDH1 program	Therapeutic targeting isocitrate dehydrogenase-1 (IDH1)	Cancer	Preclin
Myrexis Inc. (NASDAQ:MYRX)	MPC-9528	Oral NamPRT inhibitor	Cancer	Preclin; submit IND 2012
Agios Pharmaceuticals Inc.	PKM2 program	Therapeutic targeting PKM2	Cancer	Discovery

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ATP molecules per glucose molecule.

The cancer metabolism story goes back to 1924, when Otto Warburg observed what came to be called the Warburg effect: cancer cells, even in the presence of oxygen, favor glycolysis over mitochondrial oxidative phosphorylation. For years scientists wondered why cancer cells would prefer the inefficient pathway.

> ***"This drug really poisons the cell's ability to get carbons into the TCA cycle to churn out those intermediates."***
>
> **Tim Pardee, Wake Forest University**

Researchers now believe that, while less energy efficient, the pathway provides the nutrients necessary for cancer cells to generate the sugars, amino acids and lipids needed to proliferate. It also explains why cancer cells require more glucose to meet their energy needs.

Even before cancer metabolism was understood, researchers had taken advantage of the knowledge that, in some cancers, tumor cells are unable to produce particular amino acids. The first generation of drugs targeting cancer metabolism exploited this deficiency as a way of starving the tumor cell.

The first example was in acute lymphoblastic leukemia (ALL), where cancer cells depend on exogenous sources of the amino acid asparagine due to a metabolic defect in asparagine synthesis. In the 1990s, forms of asparaginase were developed that made dietary asparagine unavailable to the malignant cells.

Asparaginase converts circulating asparagine into aspartic acid, thus depriving tumor cells of the amino acid. Normal cells, which can synthesize asparagine, are unaffected by the therapy.

Merck & Co. Inc. markets Elspar asparaginase, while **Sigma-Tau Group** markets Oncaspar pegaspargase, a pegylated L-asparaginase, which it acquired from **Enzon Pharmaceuticals Inc.** in 2009.

Polaris Pharmaceuticals Inc. is taking a similar approach in hepatocellular carcinoma (HCC), which requires exogenous arginine to survive. Polaris' ADI-PEG 20 is a pegylated arginine deiminase that depletes dietary arginine. In July, the company started a Phase III trial in about 600 HCC patients.

As with the asparaginase drugs, normal cells that can synthesize arginine are left unharmed by ADI-PEG 20.

A third approach seeks to arrest tumor growth by directly blocking uptake of exogenous glucose by cancer cells.

Ruga has a series of small molecules in preclinical development that impair glucose transporter 1 (GLUT1), which is aberrantly activated in cancer cells that rely on the Warburg effect. The company has licensed the molecules from an academic team led by Amato Giaccia, professor of radiation oncology at the **Stanford University School of Medicine**.

In August 2011, Giaccia and colleagues published in *Science Translational Medicine* that the lead compound of the series, STF-31, inhibited growth of renal cell carcinoma (RCC) *in vitro*.

Playing intermediary

As interest in cancer metabolism grew, scientists focused on the energy pathways and their components. In parallel, advances in molecular biology provided researchers with the assays and tools needed to identify and better characterize individual components of these pathways.

In 2008, a team at the **University of Pennsylvania** showed that cancer cells have increased glucose uptake compared with normal cells and that cell fueling via the glycolytic pathway was associated with activated oncogenes such as ras and v-myc myelocytomatosis viral oncogene homolog (MYC; c-Myc).

Also that year, the same team identified glutamine metabolism via the TCA cycle as an important source of intermediates — or nutrients — for cancer cell biosynthesis.

Those two papers sparked interest in the field, as other groups reported the identification and characterization of other enzymes that are altered in cancer metabolism. These included pyruvate kinase M2 isozyme (PKM2), isocitrate dehydrogenase-1 (IDH1) and IDH2, pyruvate dehydrogenase (PDH) and monocarboxylate transporter 1 (MCT1).

Whereas previous approaches targeted the exogenous metabolic needs of cancer cells, the new targets were intracellular modulators of energy sources or processes required to produce intermediates.

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A case in point is pyruvate kinase, the last enzyme in the aerobic glycolytic cascade. It has two main variants: PKM1 and PKM2.

According to Dynamix President and CEO Oren Becker, non-proliferating cells express the PKM1 isoform, which is a very efficient tetramer enzyme that can rapidly convert glycolytic intermediates into pyruvate. Cells undergoing high rates of nucleic acid synthesis — such as proliferating cancer cells — express PKM2, which is much less efficient because it is in a dimer state instead of a tetramer.

Because PKM2 converts intermediates into pyruvate at a much slower rate than PKM1, Becker said the result is a bottleneck in the glycolytic pathway that leads to the buildup of intermediates along the cascade, such as carbon skeletons, that tumor cells need for biosynthesis.

> ***"Repairing DNA damage is a very energy-dependent process."***
>
> **Adrian Hobden, Myrexis Inc.**

PKM2 leads to continually increasing levels of glycolytic intermediates, including one called fructose biphosphate (FBP). Once FBP levels reach a certain threshold, FBP binds PKM2 and causes it to tetramerize, essentially converting it to PKM1. This eases the bottleneck and reduces the levels of intermediates.

"What happens is every once in a while the levels of these intermediates are high enough that FBP will flush down the system by modifying PKM2, which opens the pipe and relaxes the system," Becker said.

Dynamix thus is developing small molecules that mimic FBP to drive down levels of PKM2.

According to Becker, Dynamix's compounds should normalize the metabolism of the cancer cell and prevent it from accumulating the biomass necessary for proliferation. Becker said that in *in vitro* assays, the compounds arrest the cancer cell in the G1 phase of the cell cycle, preventing it from progressing into the synthesis phase.

The company also hopes the approach should have minimal toxicity. "In a normal cell, our small molecule may bind to PKM1, but it doesn't do anything. PKM1 is already a tetramer. So it should basically have no effect on normal cells," Becker said.

At the American Society of Clinical Oncology (ASCO) meeting in June, Dynamix presented preclinical data showing FBP mimetics significantly reduced the proliferation rate of colorectal, renal, lung, cervix and liver cancer cell lines. In a xenograft mouse model of colorectal cancer, one of the mimetics, DNX-03013, inhibited tumor growth by >50% after a few days with no side effects at high exposure levels.

The PKM2 program is expected to enter the clinic next year.

Agios also has a PKM2 program in discovery. Indeed, the PKM2 variant in cancer cells was identified in 2008 by one of the company's scientific founders, Lewis Cantley. However, Agios' lead program focuses on a different target: isocitrate dehydrogenase-1 (IDH1).

The metabolic enzyme and a related enzyme, IDH2, are mutated in about 70% of brain cancers and 25% of adult leukemias. The mutated enzymes also occur in a smaller percentage of other solid tumors.

According to CEO David Schenkein, the mutant enzymes have the ability to engage in a novel chemical reaction that creates the oncometabolite 2-hydroxyglutarate (2HG).

"When the tumor cell produces very high levels of 2HG, the oncometabolite is affecting key epigenetic enzymes that lead to hypermethylation of DNA, which in turn leads to tumorigenesis and tumor maintenance. It's an example of altered metabolism driving epigenetic changes," he said.

IDH1 and IDH2 also are involved in nicotinamide adenine dinucleotide (NAD+) production. Because NAD+ is an important source of energy for biosynthesis, the mutations in IDH1 and IDH2 also may promote cellular proliferation.

Schenkein said it's still unclear whether the energy component of IDH1 or the epigenetic changes IDH1 initiates are more important in driving tumor growth and proliferation.

The IDH1 program is in preclinical development. The company hasn't disclosed when it is expected to enter the clinic.

Agios continues to identify additional cancer metabolism targets.

In July 2011, Agios and collaborators at MIT published in *Nature* the results of an RNAi-based *in vivo* screen, which identified phosophoglycerate dehydrogenase (PHGDH) as a new target. In healthy cells, the enzyme catalyzes the first step of the serine biosynthesis pathway. However, in breast cancer cells, the enzyme is hijacked to increase production of proteins and nucleotides that are needed for proliferation *(see SciBX:Science-Business eXchange, Aug. 4)*.

In the power plant

While Agios and Dynamix are going after mutated metabolic enzymes in the cytosol, Cornerstone is looking at what happens inside the mitochondria, where the TCA cycle takes place.

The company's CPI-613 is in two Phase I trials in hematologic malignancies and solid tumors.

Mitochondria are the cellular engines that produce ATP in normal cells. In the altered metabolism of the cancer cell, however, the function of mitochondria is shifted toward producing nutrients necessary for biosynthesis.

Cancer cells use the TCA cycle to create the backbones for synthesizing amino acids and nucleotides. According to Tim Pardee, associate professor of hematology and oncology at **Wake Forest University School of Medicine**, cancer cells "turn their mitochondria from ATP factories into carbon skeleton factories for amino acids and sugar backbones for RNA and DNA. It allows them to maintain their prodigious growth rate."

An essential step is getting carbons into the TCA cycle to produce these intermediates. This is the point of Cornerstone's attack. CPI-613 targets two mitochondrial enzymes that Pardee called gateway proteins to the TCA cycle: pyruvate dehydrogenase (PDH) and alpha-ketoglutarate.

"You can't get carbons into the TCA cycle without going through one or the other," said Pardee, who is the lead investigator in CPI-613's Phase I trial for hematological malignancies.

According to CEO Rob Shorr, studies have shown that higher levels of PDH in tumor cells correlate with a higher degree of malignancy.

CPI-613 is an analog of alpha-lipoic acid, which is a necessary co-factor for PDH and alpha-ketoglutarate function. Shorr said cancer cells have a greater need for the co-factor than healthy cells because they are involved in a much higher rate of

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biosynthesis. CPI-613 therefore is preferentially taken up by tumor cells, while healthy cells tested *in vitro* do not take up the compound.

Once the lipoic acid analog is delivered to the mitochondria, Shorr said, it stimulates pyruvate dehydrogenase kinase (PDK), which turns off PDH. The activity of alpha-ketoglutarate is similarly arrested. As a result, said Pardee, "this drug really poisons the cell's ability to get carbons into the TCA cycle to churn out those intermediates."

Pardee said the cancer cell is left in an untenable position, as it's being driven by oncogenes to continually divide but doesn't have the resources to do so. He believes this tension leads to apoptotic or necrotic cell death.

At ASCO, Cornerstone presented interim Phase I data from five patients in the hematological malignancies trial, including two patients with relapsed acute myelogenous leukemia (AML). One AML patient had a reduction in peripheral blood blasts, while the second AML patient had an increase in platelet counts.

The second AML patient also showed a decrease from 50% to 32% in cells with the 7q- mutation at five cycles of treatment.

The 7q- abnormality in AML cells indicates very resistant and aggressive disease. Patients with the 7q- mutation have the worst prognosis.

No patients experienced greater than grade 2 adverse events associated with the compound.

Shorr said there's no timeline for final data, as the trial is still escalating doses.

"When a malignant cell alters its metabolic machinery, we have evidence that it leaves a metabolic profile that we can use to identify the right patients."

David Schenkein, Agios Pharmaceuticals

Deenergized

Another strategy is to cut off the cancer cell's energy supply to limit its ability to repair DNA damage.

Cancer cells have a significant amount of DNA damage that they are constantly repairing. The processes require lots of energy, specifically in the form of NAD+.

"Repairing DNA damage is a very energy-dependent process," noted Myrexis President and CEO Adrian Hobden.

Myrexis' MPC-9528 is a preclinical small molecule inhibitor of nicotinamide phosphoribosyl transferase (NamPRT), the key enzyme in the synthesis of NAD+. Inhibiting NamPRT "prevents the repair of DNA damage essentially by starving the cell of the energy," Hobden said.

While NamPRT is involved in the internal synthesis of NAD+, cells also can make NAD+ from external sources such as niacin. They do so by expressing nicotinate phosphoribosyltransferase (NAPRT1), which converts niacin to NAD+, thus bypassing the effect of NamPRT inhibition.

Hobden said all healthy cells have this rescue pathway, but about 40% of tumors do not. This means a patient lacking the pathway potentially could be given MPC-9528 in combination with niacin. The combination would inhibit NAD+ production in tumor cells, but provide healthy cells with an external source of NAD+.

Myrexis is particularly interested in glioblastoma. Hobden said none of the tumor samples examined by the company have expressed the NAPRT1 rescue pathway, which should make them sensitive to NamPRT inhibition.

Myrexis hopes to submit an IND for MPC-9528 next year. At ASCO, the company presented preclinical data from mouse fibrosarcoma xenograft models in which 75 mg/kg of MPC-9528 dosed weekly for three weeks resulted in 75% xenograft regression eight days after the last dose.

Hobden said the company has seen in subsequent preclinical studies that lower, more commercially viable doses given once or twice daily can provide similar efficacy to the higher, intermittent doses such as 75 mg/kg once weekly.

For example, 3 mg/kg twice daily, 4 mg/kg twice daily and 10 mg/kg once daily for 14 days led to 92%, 100% and 91% tumor regression, respectively, by the end of dosing. Hobden said a dose response was not expected at these levels because they were all saturating doses that produced maximal responses in the model.

The most advanced NamPRT inhibitor is **TopoTarget A/S**'s APO866, which is in Phase II testing to treat cutaneous T cell lymphoma (CTCL).

Gemin X Pharmaceuticals Inc., which was acquired by **Cephalon Inc.** in April, had the NamPRT inhibitor teglarinad (GMX1777) in a Phase I/II trial for metastatic melanoma. The trial was halted due to financial constraints. Cephalon, which is being acquired by **Teva Pharmaceutical Industries Ltd.**, said the program is under evaluation.

While Myrexis is behind competitors, Hobden thinks MPC-9528 has the potential to be best in class because it is orally bioavailable. APO866 is given intravenously.

Harnessing byproducts

When tumor cells use glycolysis to produce intermediates, the byproduct is lactate, which is then transported out of the cell.

The key enzyme in lactate transport is MCT1, which is overexpressed in many tumor types, but not in normal tissue.

AstraZeneca and CRT are developing AZD-3965 as an MCT1 inhibitor. According to Ian Walker, licensing manager for clinical partnerships at CRT, inhibiting MCT1 prevents the cancer cell from transporting lactate out of the cell. This leads to lactate buildup, causing acidosis that leads to cell death.

CRT will run a Phase I/IIa trial that is planned to begin this year. AstraZeneca has an option to reacquire rights to AZD-3965 after the study. If the option isn't exercised, CRT can out-license the compound or continue development itself.

The companies also have a three-year deal to discover small molecules against undisclosed cancer metabolism targets discovered by CRT. AstraZeneca is responsible for preclinical and clinical development, while CRT is eligible for milestones, plus royalties.

Combinations and biomarkers

All companies contacted by BioCentury said there was an opportunity for combining therapeutics targeting metabolism with cell signaling and cytotoxic therapies.

"It's likely that many of the drugs we will develop will be used

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sometimes alone, but often in combination with other conventional or novel targeting agents. And that is absolutely central and a key component of our strategy," said Agios' Schenkein.

Said Hobden: "Because our drug is inhibiting DNA repair, we predicted that some of the cancer drugs that work by inducing DNA damage should be hypersensitive in combination with MPC-9528."

Hobden said *in vitro* studies showed MPC-9528 plus 5-fluorouracil (5-FU) had significant synergy in colorectal cancer, as did MPC-9528 plus Merck's Temodar temozolomide in glioblastomas.

Dynamix's Becker thinks there is potential for a PKM2-targeted therapy to be part of a first-line regimen because converting PKM2 to PKM1 should prevent further proliferation of the cancer cells.

He also said a PKM2 therapeutic could be used as a maintenance therapy to prevent recurrence.

Agios also is developing biomarkers for its compounds before they enter the clinic.

"We should have the ability to identify the patients most likely to respond using biomarkers," Schenkein said. "When a malignant cell alters its metabolic machinery, we have evidence that it leaves a metabolic profile that we can use to identify the right patients."

For instance, measuring levels of the oncometabolite 2HG will be a key component of the company's biomarker strategy in its IDH1 and IDH2 program. Schenkein said Agios has the internal competencies to discover biomarkers but will partner with diagnostics companies to develop kits.

Similarly, Myrexis is looking to develop a diagnostic that could identify tumors lacking the NAPRT1 rescue pathway. The company has a legacy in diagnostics — it was spun out of cancer diagnostics company **Myriad Genetics Inc.** in 2009. Thus, Hobden said Myrexis would be capable of developing its own kit.

Becker said Dynamix is doing preliminary work to identify biomarkers that would indicate a tumor is highly glycolytic with high PKM2 expression.

COMPANIES AND INSTITUTIONS MENTIONED

Agios Pharmaceuticals Inc., Cambridge, Mass.
AstraZeneca plc (LSE:AZN; NYSE:AZN), London, U.K.
Cancer Research UK, London, U.K.
Cephalon Inc. (NASDAQ:CEPH), Frazer, Pa.
Cornerstone Pharmaceuticals Inc., Cranbury, N.J.
Dynamix Pharmaceuticals Ltd., Rehovot, Israel
Enzon Pharmaceuticals Inc. (NASDAQ:ENZN), Bridgewater, N.J.
Merck & Co. Inc. (NYSE:MRK), Whitehouse Station, N.J.
Myrexis Inc. (NASDAQ:MYRX), Salt Lake City, Utah
Myriad Genetics Inc. (NASDAQ:MYGN), Salt Lake City, Utah
Polaris Pharmaceuticals Inc., San Diego, Calif.
Ruga Corp., Palo Alto, Calif.
Sigma-Tau Group, Pomezia, Italy
Stanford University School of Medicine, Palo Alto, Calif.
Teva Pharmaceutical Industries Ltd. (NASDAQ:TEVA), Petah Tikva, Israel
TopoTarget A/S (CSE:TOPO), Copenhagen, Denmark
University of Pennsylvania, Philadelphia, Pa.
Wake Forest University School of Medicine, Winston-Salem, N.C.

Product Discovery & Development

Locking in lebrikizumab

By Erin McCallister
Senior Writer

In the race to treat asthma by blocking IL-13, **Genentech Inc.** now has positive Phase II data and a biomarker for responders to lebrikizumab in severe asthma patients. Next up is data from **MedImmune LLC's** tralokinumab.

IL-13 is secreted by T helper type 2 (Th2) cells and leads to JAK/STAT signaling via STAT6 (signal transducer and activator of transcription 6). This signaling activates neutrophils, which have been implicated in lung damage.

While production of IL-13 is inhibited by corticosteroids, patients with uncontrolled asthma still have high levels of the cytokine in their sputum.

According to John Matthews, senior medical director for product development inflammation at the Genentech unit of **Roche**, lebrikizumab is a human IgG 4 antibody with a stabilizing point mutation in the hinge region to increase its stability in the blood. This gives lebrikizumab a longer half-life that allows for once-monthly dosing.

> ***"We were looking for something that would really show that we have a specific drug for asthma patients."***
>
> **John Matthews, Genentech**

In the *New England Journal of Medicine* this month, Genentech reported lebrikizumab met the primary endpoint in the Phase II MILLY trial to treat asthma in adults inadequately controlled with inhaled corticosteroids.

In 218 patients, lebrikizumab dosed every four weeks significantly improved the mean relative change in forced expiratory volume in one second (FEV1) from baseline to week 12 vs. placebo (9.8% vs. 4.3%, p=0.02).

The FEV1 value was higher in a subgroup of patients with high levels of periostin. In a prespecified subgroup analysis, treated patients had a mean relative increase in FEV1 of 14% vs. 5.8% for placebo (p=0.03). The FEV1 increase for lebrikizumab in patients with low periostin was only 5.1% vs. 3.5% (p=0.61).

IL-13 induces epithelial cells to produce periostin, a matricellular protein. At the American Thoracic Society International Conference in May, Genentech, Roche and researchers at the **University of California, San Francisco** showed that periostin was the best independent predictor of persistent airway eosinophilia despite steroid treatment in moderate-severe asthmatic patients.

Increased periostin can lead to stiffening of the epithelial cell matrix and airway remodeling. It was this link between periostin and IL-13 that led Genentech to pursue lebrikizumab.

"We were looking for something that would really show that we have a specific drug for asthma patients and that we could select for patients that respond to our drug," Matthews told BioCentury.

He could not give an estimate of the proportion of severe asthma patients with high levels of periostin.

Genentech is in discussions with regulatory authorities about the Phase III program. Matthews said it is too soon to say whether the company will enroll only patients with high periostin levels.

In the meantime, Roche's diagnostic division is developing a periostin-based companion diagnostic for lebrikizumab.

MedImmune, a unit of **AstraZeneca plc**, also has a mAb against IL-13 in development — tralokinumab (CAT-354).

Neither MedImmune nor Genentech would compare their mAbs. Bing Yao, SVP and head of innovative medicine for respiratory inflammation and autoimmunity at MedImmune, said tralokinumab is potent and specific for IL-13.

He said published studies in mouse models of asthma have shown that tralokinumab neutralized airway hyperresponsiveness. He also said published Phase I studies have shown tralokinumab is safe and well tolerated, with a good pharmacokinetic profile.

The company plans to present Phase IIa data at the European Respiratory Society meeting in Amsterdam next month.

Tralokinumab was dosed every two weeks in the Phase IIa trial. The company would not disclose the frequency of dosing in the Phase IIb trial that began this year.

Yao said MedImmune is evaluating biomarkers for tralokinumab, as it is for all its programs, but he declined to say which ones.

Genentech and MedImmune are not the first to target IL-13 in asthma, but earlier attempts were not successful.

Aerovance Inc. reported last year that its inhaled Aerovant, a recombinant human IL-4 variant that inhibits both IL-4 and IL-13 receptors, failed a Phase IIb trial.

Altair Therapeutics Inc. had AIR645, an inhaled antisense inhibitor of the IL-4/IL-13 signaling pathways. The company, which licensed the molecule from **Isis Pharmaceuticals Inc.**, ceased operations in February. Isis has reacquired the asset, but has no plans to develop the program.

Matthews noted the proportion of IL-13 is much higher than IL-4 in severe asthma. Instead, he said, IL-4 secretion is often associated with early development of asthma.

He suggested that systemic delivery may result in more consistent dosing than inhaled administration.

Asthma attack

Lebrikizumab could give Roche two marketed mAbs for severe asthma. The pharma markets Xolair omalizumab for the indication.

Xolair had 2010 sales of CHF641 million ($684 million), up from CHF620 million ($602 million) in 2009.

Genentech spokesperson Christopher Vancheri said it is too early to say how lebrikizumab might complement the recombinant humanized mAb against IgE.

Other Roche asthma candidates include RG7449, a mAb against the M1 prime segment of membrane IgE that is in

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Phase II testing, and RG7185, a small molecule antagonist of prostaglandin D2 (PGD2) receptor (CRTH2; GPR44; CD294) that is in Phase I testing.

Unlike lebrikizumab, which helps to reduce the inflammatory response associated with asthma, RG7449 has the ability to induce antibody-dependent cell cytotoxicity, and thus could be disease modifying, Vancheri said. Both are delivered via injection.

RG7185, on the other hand, would give the company an oral option over the injectable antibodies.

Lebrikizumab also is being explored for idiopathic pulmonary fibrosis (IPF), though the company hasn't decided whether to pursue this indication, Vancheri said.

COMPANIES AND INSTITUTIONS MENTIONED

Aerovance Inc., Berkeley, Calif.
AstraZeneca plc (LSE:AZN; NYSE:AZN), London, U.K.
Genentech Inc., South San Francisco, Calif.
Isis Pharmaceuticals Inc. (NASDAQ:ISIS), Carlsbad, Calif.
MedImmune LLC, Gaithersburg, Md.
Roche (SIX:ROG; OTCQX:RHHBY), Basel, Switzerland
University of California, San Francisco, San Francisco, Calif.

Daclizumab in MS

Biogen Idec Inc. (NASDAQ:BIIB) and partner **Abbott Laboratories** (NYSE:ABT) last week reported top-line Phase IIb data for daclizumab that appear better than interferons and comparable to oral compounds for relapsing-remitting multiple sclerosis (RRMS). The once-monthly, subcutaneous formulation of the humanized mAb against IL-2 receptor alpha chain (CD25), dubbed DAC HYP, led to a 54% relative reduction in annualized relapse rate (ARR) and a 57% improvement in Expanded Disability Severity Scale (EDSS).

However, the robust efficacy was tempered by two deaths, along with a higher rate of adverse events. One death was due to a complication of a psoas muscle abscess in a patient recovering from a serious skin adverse event, and the other was in the ongoing SELECTION extension study due to possible autoimmune hepatitis. The companies said they could not exclude a contributory role for DAC HYP. In addition, patients given DAC HYP had a higher incidence of infections, serious cutaneous events and liver abnormalities vs. placebo.

Biogen Idec is not saying when the full results will be released. In May, CEO George Scangos told BioCentury SELECT would be one of two registrational trials. DAC HYP also is being compared with Avonex in the Phase III DECIDE trial, which is expected to complete in 2013 or early 2014.

Biogen Idec is piling up shots on goal in RRMS. It has BG-12, an oral dimethyl fumarate, and PEG-IFN, a pegylated interferon beta-1a, in Phase III testing. Data from CONFIRM, the second of two Phase III trials of BG-12, are expected this half. Data from the ADVANCE trial of PEG-IFN given once or twice monthly are expected in 2013.

"If once a month subcutaneous dosing were to work, then I think it's a legitimate question to ask whether that is more or less convenient than the daily pill," Scangos told BioCentury. "If it were me, I might rather get a subcutaneous injection once a month than worry about the pills every day."

Roche (SIX:ROG; OTCQX:RHHBY) marketed daclizumab as Zenapax to prevent transplant rejection, but withdrew the product in 2009 due to low demand. (A) ARR except for Copaxone, which is mean number of relapses over two years; (B) Reduction in relative risk of sustained disease progression using EDSS unless otherwise noted; IV = intravenous; SC = subcutaneous; *Sources: Annals of Neurology; The Lancet; FDA briefing documents; drug labels; company press releases and presentations*

Trial		Compound (n)	ARR (A)	Relative reduction vs. control	EDSS improvement (B)	Safety
Marketed drugs						
Avonex interferon beta-1a (IV) from **Biogen Idec Inc.** (NASDAQ:BIIB)						
2-year Study 1	MS with at least 2 relapses in the past 3 years	Avonex (158) Placebo (143)	0.61 0.90	32% [p=0.02] for patients completing 2 yrs of treatment	37% [p=0.02]	Flu-like symptoms: myalgia, fever, fatigue, headaches, chills, nausea and vomiting
Copaxone glatiramer (SC) from **Teva Pharmaceutical Industries Ltd.** (NASDAQ:TEVA)						
2-year Study 2	MS with at least 2 exacerbations in the 2 years before the start of the study	20 mg/day Copaxone (125) Placebo (126)	1.19 1.68	29% [p=0.055]	NA	Most common adverse reactions included injection site reactions, vasodilatation, rash, dyspnea, and chest pain
Gilenya fingolimod (oral) from **Novartis AG** (NYSE:NVS; SIX:NOVN)/**Mitsubishi Tanabe Pharma Corp.** (Tokyo:4508; Osaka:4508)						
2-year Phase III FREEDOMS	MS with at least 1 relapse in past year or at least 2 relapses in past 2 years	0.5 mg Gilenya (425) 1.25 Gilenya (429) Placebo (418)	0.18 0.16 0.40	54% 60%	30% [p=0.024] 32% [p=0.017]	CV abnormalities seen at first dose: 48% of patients in the 1.25 mg arm had a pulse rate drop, 33% in 0.5 mg arm; increased rate of macular edema in 1.25 mg arm; drops in FEV1 and diffusion capacity for carbon monoxide in both Gilenya arms vs. placebo
1-year Phase III TRANSFORMS	MS with at least 1 relapse in past year or at least 2 relapses in past 2 years	0.5 mg Gilenya (429) 1.25 Gilenya (420) Avonex (431)	0.16 0.20 0.33	52% 38%	NA	
Tysabri natalizumab (IV) from **Biogen Idec Inc.** (NASDAQ:BIIB) / **Elan Corp. plc** (NYSE:ELN)						
2-year Study MS1	MS with at least 1 relapse in past year	300 mg Tysabri every 4 wks (627) Placebo (315)	0.22 0.67	67%	42%	Black box warning on label stating Tysabri increases the risk of progressive multifocal leukoencephalopathy (PML)
2-year Study MS2	MS with at least 1 relapse while on treatment with Avonex once weekly during the year prior to study entry	300 mg Tysabri every 4 wks (589) Placebo (582)	0.33 0.75	56%	24%	

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Trial		Compound (n)	ARR (A)	Relative reduction vs. control	EDSS improvement (B)	Safety
Phase III compounds						
BG-12 (oral) from **Biogen Idec Inc.** (NASDAQ:BIIB)						
2-year Phase III DEFINE	MS with at least 1 relapse in past year and a previous cranial MRI showing lesions consistent with MS, or gadolinium-enhancing lesions on MRI within past 6 weeks	240 mg BG-12 twice daily 240 mg BG-12 thrice daily Placebo *Total patients >1,200*	NA NA	53%	38%	Detailed data not available
Lemtrada alemtuzumab (IV) from **Sanofi** (Euronext:SAN; NYSE:SNY) / **Bayer AG** (Xetra:BAY)						
2-year Phase III CARE-MS I	MS with at least 2 exacerbations in past 2 years, and at least 1 exacerbation in past year	5-day cycle/year Lemtrada Rebif IFN beta-1a thrice weekly	NA NA	55% [p<0.0001]	8% of Lemtrada patients had sustained increase in EDSS score at 2 yrs vs. 11% for placebo [p=0.22]	Headache, rash, fever, nausea, flushing, hives and chills; incidence of infections was also increased in Lemtrada patients
Daclizumab high-yield process (SC) from **Biogen Idec Inc.** (NASDAQ:BIIB) / **Abbott Laboratories** (NYSE:ABT)						
1 year Phase IIb SELECT	MS with at least 1 relapse in past year and a previous MRI showing lesions consistent with MS, or gadolinium-enhancing lesions on MRI within past 6 weeks	150 mg daclizumab 300 mg daclizumab Placebo *Total patients = 600*	NA NA NA	54% [p<0.0001] 50% [p=0.0002]	57% 43%	Serious infections (2% daclizumab vs. 0% placebo); serious cutaneous events (1% vs. 0%); liver function test abnormalities >5 times the upper limit of normal (4% vs. <1%)
Laquinimod (oral) from **Active Biotech AB** (SSE:ACTI) / **Teva Pharmaceutical Industries Ltd.** (NASDAQ:TEVA)						
2-year Phase III ALLEGRO	MS with at least 1 relapse in past year or at least 2 relapses in past 2 years or at least 1 relapse between 1-2 years and at least 1 gadolinium-enhancing lesion in the past year	0.6 mg laquinimod (550) Placebo (556)	NA	23% [p=0.0024]	36% [p=0.012]	Increased ALT (6.9% laquinimod vs. 2.7% placebo); abdominal pain (5.8% vs. 2.9%); back pain (16.4% vs. 9%); cough (7.5% vs. 4.5%); urinary tract infection (7.3% vs. 4.5%); diarrhea (8% vs. 6.1%); headache (22.7% vs. 17.8%)
2-year Phase III BRAVO	IFN-naïve MS with at least 1 relapse in past year or at least 2 relapses in past 2 years or at least 1 relapse between 1-2 years and at least 1 gadolinium-enhancing lesion in the past year	0.6 mg laquinimod Placebo *Data adjusted for baseline MRI dissimilarities; total patients = 1,331*	0.28 0.34	21% [p=0.026]	34% [p=0.044]	Comparable to ALLEGRO; no new safety signals and no signs of immunosuppression
Teriflunomide (oral) from **Sanofi** (Euronext:SAN; NYSE:SNY)						
2-year Phase III TEMSO	MS with at least 1 relapse in past year, or at least 2 relapses in past 2 years	7 mg teriflunomide 14 mg teriflunomide Placebo *Total patients = 1,088*	0.37 0.36 0.54	31% [p=0.0002] 31% [p=0.0005]	24% [p=0.0835] 30% [p=0.0279] Risk reduction of 12-wk disability progression	Both doses were well tolerated, with diarrhea, nausea, elevations in ALT, and mild hair thinning and hair loss occurring more frequently in teriflunomide-treated patients vs. placebo

Emerging Company Profile

Verastem: Cancer stem cell engine

By Andrew Fisher
Staff Writer

Cancer stem cells have long been recognized as important therapeutic targets, but growing enough of them to allow for screening with typical drug discovery methods has been a challenge. **Verastem Inc.** believes its techniques have removed the bottleneck to high throughput screening.

Cancer stem cells (CSCs), which often remain after treatment with chemo- or radiotherapies, are believed to be responsible for disease recurrence and can migrate through the body to form metastases.

Verastem uses a procedure developed by co-founder Piyush Gupta and colleagues that forces cancer cells to undergo epithelial-mesenchymal transition (EMT). Co-founder Robert Weinberg said cells undergoing EMT "acquire a 'stem-ness'" that includes increased motility, the ability to form new cancers, and an increased resistance to chemotherapies — all properties of CSCs.

With the ability to drive cells through EMT, Verastem can produce an almost unlimited number of its CSCs for screening.

Using libraries exclusively licensed from the **Broad Institute** and the **Whitehead Institute for Biomedical Research**, the company has screened more than 300,000 compounds and found four with increased selectivity for CSCs over normal cancer cells.

One of the Verastem compounds, VS-507, is a proprietary formulation of salinomycin being developed to treat breast cancer. The selective potassium ionophore is marketed as a generic veterinary antibiotic. Verastem said the exact mechanism by which VS-507 kills CSCs has not been determined.

Weinberg and colleagues have shown that salinomycin reduced the proportion of CSCs in breast cancer cells by more than 100-fold compared with paclitaxel. In a mouse model of breast cancer, salinomycin inhibited tumor growth and metastasis compared with paclitaxel. Data were published in *Cell* in 2009.

COO Robert Forrester said the company is screening for additional compounds, including NCEs.

Verastem Inc.

Boston, Mass.

Technology: Therapeutics targeting cancer stem cells

Disease focus: Cancer

Clinical status: Preclinical

Founded: 2010 by Richard Aldrich, Piyush Gupta, Satish Jinal, Eric Lander, Robert Weinberg and Christoph Westphal

University collaborators: Harvard University and Massachusetts Institute of Technology

Corporate partners: NA

Number of employees: 15

Funds raised: $48 million

Investors: Advanced Technology Ventures, Astellas Venture Management, Bessemer Venture Partners, Cardinal Partners, Longwood Founders Fund and MPM Capital

CEO: NA

Patents: 3 issued covering methods for screening for compounds that target cancer stem cells and use of these compounds to treat cancer

While Verastem has not picked a lead, the company hopes to begin Phase I/II testing next year of at least one molecule to treat triple-negative breast cancer in patients with low levels of claudin. Low levels of claudin-1 (CLDN1) have been implicated in increased risk of metastasis.

According to Forrester, these patients have few treatment options because their cancers are resistant to current therapies, and because CSCs make up 30-50% of their tumors.

Forrester said Verastem likely will pursue subsets of patients with other types of solid tumors based on the "biology underlying tumor recurrence and the role of cancer stem cells within the most aggressive tumors." Weinberg added that the company plans to pair its anti-CSC agents with chemotherapy to kill both CSCs and conventional cancer cells.

Verastem also is developing a proprietary EMT signature as a companion diagnostic to monitor patients during clinical trials. The company envisions using biomarkers of mesenchymal cells instead of reduced tumor volume to measure the effect of its compounds. The assay also could be used to identify tumors that have a high proportion of CSCs.

Verastem has about $45 million in cash, which Forrester said should take one to two compounds through Phase II testing in the next 2-3 years. The company plans on taking its compounds through Phase II without a partner.

At least two other companies targeting CSCs have compounds in the clinic. **Boston Biomedical Inc.**'s BBI608 is in Phase Ib/II testing for solid tumors and Phase I for colorectal cancer. **Dainippon Sumitomo Pharma Co. Ltd.** has an option to the small molecule CSC inhibitor against an undisclosed molecular target.

This year, **OncoMed Pharmaceuticals Inc.** began a Phase I trial of OMP-59R5 to treat advanced solid tumors. **GlaxoSmithKline plc** has an option to the mAb that binds selected Notch receptors under a 2007 deal to identify mAbs against CSCs.

According to Forrester, other companies targeting CSCs design molecules against a specific target. In contrast, Verastem thinks its ability to generate a stable pool of CSCs will allow it to look for compounds that show activity against the tumor, regardless of the specific target.

"We're taking the premise that we'll let the biology direct us to the right chemistry," he said.

COMPANIES AND INSTITUTES MENTIONED

Boston Biomedical Inc., Norwood, Mass.
Broad Institute, Cambridge, Mass.
Dainippon Sumitomo Pharma Co. Ltd. (Tokyo:4506; Osaka:4506), Osaka, Japan
GlaxoSmithKline plc (LSE:GSK; NYSE:GSK), London, U.K.
OncoMed Pharmaceuticals Inc., Redwood City, Calif.
Verastem Inc., Boston, Mass.
Whitehead Institute for Biomedical Research, Cambridge, Mass.

Ebb & Flow

Flurry for Forest finale

By Stacy Lawrence
Senior Writer

In a flurry of filings, activist investor Carl Icahn and his latest life sciences target **Forest Laboratories Inc.** (NYSE:FRX) postured for investors ahead of the company's annual meeting on Thursday this week. At least three proxy advisory services weighed in, mostly in support of company board nominees.

The adversaries, who have been trading barbed filings for several months, each fine-tuned their arguments concerning Forest's stock performance and fundamentals, and the qualifications of the competing board nominees.

Last week, Icahn noted that Forest's market cap has dropped to $9.3 billion from $26.6 billion in the past seven years, which he pointed out is the average tenure of the newest Forest directors. He added that valuations for the company's specialty pharma peer group increased during that period.

Icahn, who held a 9.2% stake at Aug. 10, nominated four directors in June: Alexander Denner, Richard Mulligan, Lucian Bebchuck and Eric Ende.

Two proxy advisory services, Institutional Shareholder Services (ISS) and Egan Jones, came out in support of all 10 Forest nominees, including three new independent directors: Christopher Coughlin, former EVP and CFO of **Tyco International Ltd.** (NYSE:TYC); Gerald Lieberman, former president and COO of investment firm **AllianceBernstein Holding L.P.** (NYSE:AB); and Brenton Saunders, CEO of **Bausch + Lomb Inc.**

Forest is expanding the board from nine to 10 seats. Icahn had noted that four of the nine current directors are insiders.

Another proxy service, Glass Lewis, recommended shareholders choose Mulligan, singling out his experience on the boards of **Biogen Idec Inc.** (NASDAQ:BIIB) and **Enzon Pharmaceuticals Inc.** (NASDAQ:ENZN). It noted the shares of both companies have risen during Mulligan's tenure.

Glass Lewis did not back Denner, who also serves on those boards, or the other two Icahn nominees. The proxy service didn't release its full report and could not be reached for comment.

Forest said it has concerns about potential conflict of interest for Denner and Mulligan due to their service on the boards of Biogen Idec and **Amylin Pharmaceuticals Inc.** (NASDAQ:AMLN). Although it doesn't market products in overlapping markets with these companies, Forest said it continues to evaluate potential acquisitions and partnerships in competitive indications.

Next nine

In last week's filings, Icahn reiterated that his proposed slate would help Forest address the upcoming patent expirations for antidepressant Lexapro escitalopram and Alzheimer's disease (AD) drug Namenda memantine.

Lexapro represented 55% of product sales for FY11 and its patent expires in March 2012. Namenda accounted for 30% of FY11 product sales and faces patent expiry in April 2015.

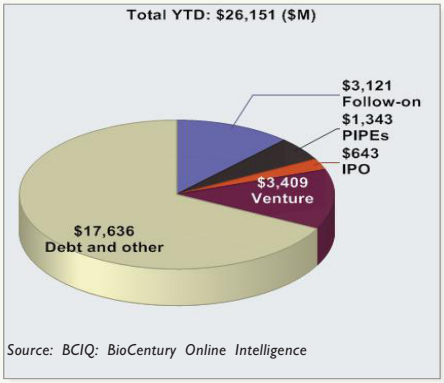
Forest noted that it has launched five new drugs since 2008, with an additional four launches planned by 2013 as part of its "Next Nine" strategy. Icahn made no mention of recent or upcoming Forest product launches in his proxy materials.

One of those launches could be for linaclotide, for which Forest and partner **Ironwood Pharmaceuticals Inc.** (NASDAQ:IRWD) announced the submission of an NDA to FDA last week. The partners are seeking approval to treat chronic constipation and irritable bowel syndrome with constipation (IBS-C).

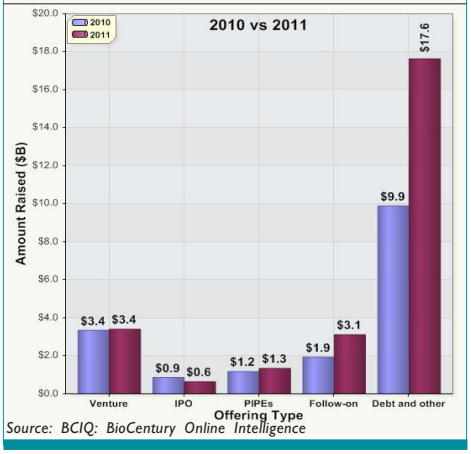
Forest finished last week up $0.53 to $34.25. Ironwood was off $1.44 (10%) to $12.46.

Money Raised in 2011

Last week, the biotech industry raised $174 million, bringing to $26.2 billion the total raised year-to-date. In 2010, a total of $36.1 billion was raised, including $23.6 billion in debt and other fundraising, $3.5 billion in follow-ons, $2.1 billion in PIPEs, $1.6 billion in IPOs, and $5.4 billion in venture capital. Totals include overallotments and warrants, and are rounded to the nearest millions.



Source: BCIQ: BioCentury Online Intelligence



Source: BCIQ: BioCentury Online Intelligence

Calm investment

Venture investors expect a $14 million series B1 round for respiratory play **Pulmatrix Inc.** will get its lead candidate to Phase IIa data in chronic obstructive pulmonary disease (COPD) and cystic fibrosis (CF).

All of Pulmatrix's existing VCs participated, including Polaris Venture Partners; 5AM Ventures; Arch Venture Partners; and Novartis Venture Fund.

Pulmatrix's lead is PUR118, which is in two Phase Ib trials in COPD. Data are expected in 1Q12.

The company's inhaled cationic airway lining modulators (iCALM) have both anti-infective and anti-inflammatory effects, Arch's Steven Gillis noted. He said this "bodes well for use in upper respiratory diseases where that type of action is warranted and could lead to a change in existing therapy."

iCALMs are designed to activate the assembly of endogenous proteins, which should result in enhanced barrier function of the lung and reduced penetration of pathogens into the lung tissue.

Pulmatrix also has three preclinical respiratory candidates.

Gillis said Arch likes to invest in platform companies with multiple shots on goal.

Pulmatrix has raised $60 million in ven-

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ture capital, plus over $10 million in grants from the **Defense Advanced Research Projects Agency** (DARPA) and the **National Institute of Allergy and Infectious Diseases** (NIAID).

Gillis said Pulmatrix may look to partner after Phase IIa testing.

Validating Vaxxas

HealthCare Ventures, an early stage investor with a penchant for academic spinouts, recently made its first Australian investment in new vaccine company **Vaxxas Pty Ltd.**

The Cambridge, Mass., firm participated in Vaxxas' first venture round, which raised A$15 million ($16.6 million). The round was led by Australian VC OneVentures. Brandon Capital Partners; the Medical Research Commercialization Fund (MRCF); and the Brisbane Angels also participated.

Vaxxas is developing a needle-free Nanopatch vaccine delivery technology. The expectation is that the technology would make it possible to use doses only 1/150th of those required for an injectable, and would not require adjuvants to boost immunogenicity.

In addition, the patch would not require refrigeration. The company said keeping vaccines cold contributes about 14% of their cost and impedes use in developing countries.

Douglas Onsi of HealthCare Ventures told Ebb & Flow the investors hope the financing will get the company to proof-of-concept (POC) data that could be the basis of a partnership with a large vaccine maker. He joined the company's board, along with Paul Kelly of OneVentures and Stephen Thompson of Brandon Capital.

Onsi said Vaxxas is talking to potential partners about what vaccines they are targeting and what data they would view as appropriate for POC.

Based on these initial conversations, he said influenza and HPV are the first two likely candidates the company will pursue.

Vaxxas founder Mark Kendall previously commercialized vaccine technology at PowderMed Ltd., which **Pfizer Inc.** (NYSE:PFE) acquired in 2006 for an undisclosed amount.

Analyst tracks

Jim Birchenough joined **BMO Capital Markets** as a managing director in the healthcare equity research group. He was the director of U.S. biotechnology equity research at Barclays Capital.

Regulatory milestones

Adventrx Pharmaceuticals Inc. (NYSE-A:ANX) was off $1.48 (58%) to $1.06 on Wednesday after receiving a complete response letter from FDA for an NDA for Exelbine vinorelbine injectable emulsion to treat non-small cell lung cancer (NSCLC). According to the company, FDA said the authenticity of the drug products used in Adventrx's bioequivalence trial could not be verified following inspections at clinical sites. The agency said the trial will need to be repeated. Adventrx lost $1.40 (57%) to $1.06 for the week.

Affymax Inc. (NASDAQ:AFFY) fell $0.68 (13%) to $4.51 last week, when FDA set a March 27, 2012, PDUFA date for an NDA for peginesatide to treat anemia in chronic kidney disease (CKD) patients on dialysis. Affymax also received a $10 million milestone from partner **Takeda Pharmaceutical Co. Ltd.** (Tokyo:4502). The milestone was triggered by FDA's acceptance of the NDA, which Affymax announced last month.

Amylin Pharmaceuticals Inc. (NASDAQ:AMLN) lost $0.49 to $10.11 last week after FDA accepted an NDA resubmission for once-weekly Bydureon exenatide for Type II diabetes. The PDUFA date is Jan. 28, 2012. Amylin and **Eli Lilly and Co.** (NYSE:LLY) developed Bydureon, which uses drug delivery technology from **Alkermes Inc.** (NASDAQ:ALKS). Alkermes was off $0.91 to $14.67.

Gilead Sciences Inc. (NASDAQ:GILD) shed $0.33 to $37.43 last week after FDA approved an NDA for Complera emtricitabine/rilpivirine/tenofovir to treat HIV-1 infection in treatment-naive patients. The product is a fixed-dose combination of Edurant rilpivirine from **Johnson & Johnson** (NYSE:JNJ) and Gilead's Truvada emtricitabine/tenofovir.

Neoprobe Corp. (NYSE:NEOP) was up $0.23 (10%) to $2.52 last week after submitting an NDA to FDA for Lymphoseek tilmanocept for use in intraoperative lymphatic mapping.

Teva Pharmaceutical Industries Ltd. (NASDAQ:TEVA) was off $1.02 to $39.70 last week after FDA accepted for review an NDA for beclomethasone dipropionate nasal aerosol to treat seasonal and perennial allergic rhinitis. The PDUFA date is March 24, 2012. Teva markets an orally inhaled formulation as Qvar for asthma.

Clinical milestones

Adolor Corp. (NASDAQ:ADLR) gained a penny to $2.31 last week after ADL5945 met the primary endpoint of the weekly average number of spontaneous bowel movements vs. placebo in two Phase II trials to treat opioid-induced constipation (OIC). The company has exclusive, worldwide rights to develop and commercialize ADL5945 from **Eli Lilly and Co.** (NYSE:LLY).

Arena Pharmaceuticals Inc. (NASDAQ:ARNA) gained $0.18 (14%) to $1.45 on Tuesday after it and partner **Eisai Co. Ltd.** (Tokyo:4523; Osaka:4523) reported on a re-adjudication of female rat mammary tumor diagnoses for lorcaserin. The data from a two-year carcinogenicity study showed the percentage of malignant tumors was lower for all dose groups of the obesity candidate than in the initial report included in Arena's 2009 NDA. The companies hope the data will address FDA's concerns about an increased rate of mammary tumors in female rats, which the agency raised in a complete response letter last October *(see B15)*.

Arena, plans to respond to the letter by year end, was off $0.08 to $1.30 for the week.

Biogen Idec Inc. (NASDAQ:BIIB) lost $2.20 to $90.98 last week after it and partner **Abbott Laboratories** (NYSE:ABT) said once-monthly subcutaneous daclizumab met the primary endpoint of annualized relapse rate compared to placebo in the Phase IIb SELECT trial to treat relapsing-remitting multiple sclerosis *(see Daclizmab in MS, A15)*.

MannKind Corp. (NASDAQ:MNKD) gained $0.42 (18%) to $2.79 on Friday after FDA confirmed the protocols of a pair of Phase III trials of Afrezza in Type I and Type II diabetes that the agency requested in a January complete response letter. The trials of the dry powder formulation of insulin plus an inhaler are expected to begin this quarter and to complete by year end 2012, with an NDA resubmission slated for about two months thereafter *(see B19)*.

MannKind was up $0.12 for the week.

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Alere Inc. (NYSE:ALR) lost $1.36 to $24.57 last week after it began an unsolicited tender offer to acquire fellow diagnostics company **Axis-Shield plc** (LSE:ASD; OSE:ASD) for 460p per share in cash. On Thursday, Axis-Shield said it continues to believe the offer undervalues the company. Investors appeared to agree: Axis Shield was up 20p to 478p on the week. On the Oslo Stock Exchange, the stock gained NOK1.10 to NOK42.10.

AMAG Pharmaceuticals Inc. (NASDAQ:AMAG) lost $0.85 to $14.97 last week after its board unanimously rejected an unsolicited offer from shareholder MSMB Capital Management to acquire the company for $18 per share, or about $380.9 million in cash. AMAG said its board determined that MSMB's proposal "is not reasonably expected to result in a superior offer" to AMAG's planned merger with cancer company **Allos Therapeutics Inc.** (NASDAQ:ALTH). Allos was off a penny to $1.74.

AnGes MG Inc. (Tokyo:4563) gained ¥5,100 to ¥73,400 last week after partnering with **GenoLac BL Corp.** to co-develop an HPV vaccine targeting E7 transforming protein (human papillomavirus-16; HpV16gp1). Details were not disclosed.

Array BioPharma Inc. (NASDAQ:ARRY) gained $0.08 to $2.23 last week after partnering with **Genentech Inc.** to develop each company's oral checkpoint kinase 1 (Chk1) inhibitor for cancer. The deal includes Genentech's GDC-0425 (RG7602), which is in Phase I testing, and Array's ARRY-575, for which an IND will be submitted next quarter.

Genentech, a unit of **Roche** (SIX:ROG; OTCQX:RHHBY), will be responsible for all clinical development and commercialization. Array will receive $28 million up front and is eligible for up to $685 million in milestones, plus double-digit royalties.

Infectious disease company **Pharmasset Inc.** (NASDAQ: VRUS) gained $15.15 (15%) to $117.65 on Tuesday after saying its board authorized a 2-for-1 stock split in the form of a 100% common stock dividend. Pharmasset was up $18.54 (17%) to $125.03 for the week.

TrovaGene Inc. (Pink:TROV) $0.26 (49%) to $0.79 last week after regaining rights to its transrenal technology from **Sequenom Inc.** (NASDAQ:SQNM). TrovaGene (formerly Xenomics Inc.) regains rights to patents covering transrenal fetal nucleic acids found in maternal urine for noninvasive prenatal and cancer diagnostics *(see B24)*.

Separately, Sequenom granted LifeCodexx AG European rights to patents covering the development of prenatal aneuploidy tests using fetal DNA in maternal plasma. Under the five-year deal, the partners will co-develop and commercialize a Trisomy 21 diagnostic test and other aneuploidy tests in Germany, Austria, Switzerland and Liechtenstein. Sequenom will receive an undisclosed upfront payment and is eligible for royalties. LifeCodexx is a subsidiary of **GATC Biotech AG**.

Sequenom lost $0.31 to $5.56 on the week.

— Staff Writer Andrew Fisher contributed to this week's Ebb & Flow

Featured links this week

Links to the following documents reside online on the BioCentury on BioBusiness page of www.biocentury.com.

Biomarkers

— FDA guidance outlining the context, structure and format of biomarker qualification submissions *(see BioCentury Extra, Thursday, Aug. 11)*.
— U.K.'s Human Genetics Commission report recommending U.K. research councils and other funding agencies review their licensing requirements for gene and biomarker patents *(see BioCentury Extra, Monday, Aug. 8)*.

Biosimilars

Minutes from the July 11 meeting between FDA and industry stakeholders for the 351(k) user fee program for biosimilars *(see BioCentury Extra, Monday, Aug. 8)*.

Clinical trials

EMA draft reflection papers on risk-based quality management and use of interactive response technologies in clinical trials.

Compliance

EMA list of all products with centralized marketing authorization that require a notification of change before an update can be made to annexes of the label.

Influenza

EMA guidance on content of variation applications for live attenuated influenza vaccines, and overview of comments received.

M&A

HBM Partners report on biotech and pharma M&A activity in 1H11 *(see BioCentury Extra, Friday, Aug. 12)*.

PMDD

EMA guideline for treatment of premenstrual dysphoric disorder (PMDD), and overview of comments received.

Product documentation

— Avastin: CHMP revised EPAR updating SPC to revise wording on congestive heart failure to include an increased incidence of CHF with a cumulative doxorubicin dose greater than 300 mg/m^2 for Avastin bevacizumab to treat breast cancer, non-small cell lung cancer (NSCLC) and metastatic renal cell cancer; from the **Genentech Inc.** unit of **Roche** (SIX:ROG; OTCQX:RHHBY).
— Integrilin: CHMP revised EPAR updating SPC to include information about potential immune related thrombocytopenia for Integrilin eptifibatide to prevent a myocardial infarction; from **Merck & Co. Inc.** (NYSE:MRK).
— RoActemra: NICE preliminary appraisal asking for additional data on the use of RoActemra tocilizumab to treat systemic juvenile idiopathic arthritis in patients who have responded inadequately to NSAIDs, systemic corticosteroids and methotrexate; from **Roche** (SIX:ROG; OTCQX:RHHBY) *(see BioCentury Extra, Tuesday, Aug. 9)*.
— Sycrest: CHMP revised EPAR updating SPC to include information on hypersensitivity reactions with Sycrest asenapine to treat moderate to severe manic episodes associated with bipolar I disorder; from **Merck & Co. Inc.** (NYSE:MRK).

EPS Watch

At least nine biotechs and pharmas reported earnings last week. **Salix Pharmaceuticals Ltd.** (NASDAQ:SLXP) lost $212 million in market value, or 10%, despite beating the Street's EPS estimate. While the company's topline was up 42% to $133.2M, helped by strong sales from its laxative products, sales of Xifaxan rifaximin came in at $87M, below analyst consensus of $91M. Xifaxan is marketed for hepatic encephalopathy (HE) and travelers' diarrhea. Salix also announced an FDA advisory committee will meet in November to discuss an sNDA for Xifaxan to treat irritable bowel syndrome (IBS). (A) EPS for 4Q ended June 30; Mcap in $M

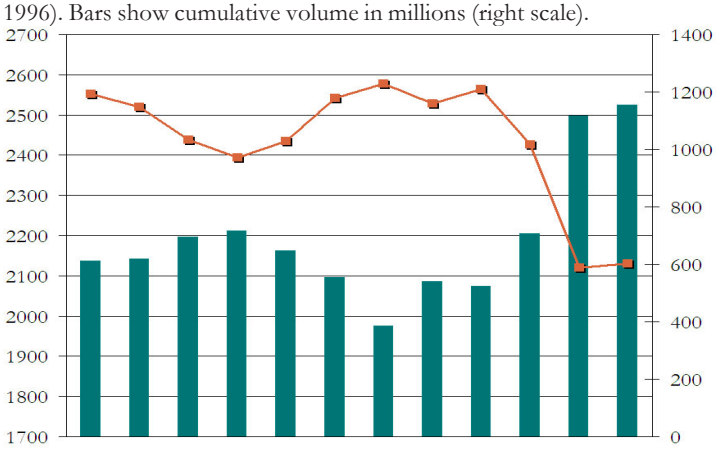
Company	2Q11 EPS est	2Q11 EPS actual	Outcome	Growth from 2Q10	8/12 cls	Wk chg	% chg	Mcap chg	8/12 Mcap
Endo Pharmaceuticals Holdings Inc. (NASDAQ:ENDP)	$1.06	$1.05	Missed by $0.01	30%	$33.49	-$0.40	-1%	-$46.6	$3,904.5
2Q11 revenues were $607.6M, up 53% from $396.5M in 2Q10. The Street was expecting $596.4M. Sales from branded pharmaceuticals were up 8% to $398.3M, helped by sales growth of 64% for pain drug Opana ER oxymorphone. Sales from generics rose 381% to $133M. Non-GAAP SG&A expenses rose 37% to $177.2M. The company raised FY11 revenue and non-GAAP EPS guidance to $2.72-$2.8B from $2.35-$2.45B and to $4.55-$4.65 from $4.20-$4.30, respectively.									
Evotec AG (Xetra:EVT)	NA	€0.01	NA	0%	2.02	0.18	10%	$29.7	$333.5
1H11 revenues from its discovery alliances rose 34% to €33.4M ($48.3M). The company raised its FY11 revenue guidance to €70-72M from €68-70M.									
Ligand Pharmaceuticals Inc. (NASDAQ:LGND)	NA	-$0.05	NA	NA	$12.13	$0.48	4%	$9.4	$238.6
Ligand reported a loss per share of $0.01 in 2Q10. 2Q11 revenues rose 28% to $7.5M from $5.8M in 2Q10. The company attributed the increase in part to sales of drug formulation technology Captisol, which it gained through its January acquisition of CyDex Pharmaceuticals Inc. Ligand confirmed its FY11 revenue guidance of $22-$24M.									
Luminex Corp. (NASDAQ:LMNX)	$0.06	$0.11	Beat by $0.05	450%	$22.04	$2.36	12%	$99.8	$932.1
2Q11 sales were $47.6M, up 43% from $33.2M in 2Q10. Sales of consumables rose 90% to $18.4M. The bioassay provider raised its FY11 revenue guidance to $180-$185M from $163-$170M.									
Myriad Genetics Inc. (NASDAQ:MYGN) (A)	$0.29	$0.30	Beat by $0.01	-44%	$18.59	-$0.75	-4%	-$64.6	$1,601.4
4Q11 EPS included a $16.1M income tax expense, which Myriad expects to offset with tax credits and loss carry forwards, while 4Q10 EPS included a one-time income tax benefit of $14.6M and no tax expense. 4Q11 revenue increased 14% to $107.4M from $93.9M in 4Q10. BRACAnalysis product revenues were $92.8M, a 12% increase from $82.5M in the previous year's quarter. Companion diagnostic service revenue grew to $2M in the quarter as a result of the May acquisition of Rules-Based Medicine Inc. Myriad introduced FY12 revenue and EPS guidance of $445-$465M and $1.20-$1.25, respectively.									
Salix Pharmaceuticals Ltd. (NASDAQ:SLXP)	$0.49	$0.54	Beat by $0.05	125%	$31.02	-$3.58	-10%	-$211.5	$1,832.7
2Q11 net product revenues were $133.2M, up 42% from $93.8M in 2Q10. Sales of hepatic and infectious drug Xifaxan rifaximin rose 20% to $87M, but below analyst consensus of $91M. Sales from the company's colon cleansing drugs business rose 353% to $27.6M. The company continues to expect FY11 revenues of $520M.									
SciClone Pharmaceuticals Inc. (NASDAQ:SCLN)	$0.10	$0.03	Missed by $0.07	-73%	$5.18	-$0.74	-13%	-$43.2	$302.1
Total revenues rose 60% to $33.1M from $20.7M in 2Q10. SciClone markets Zadaxin thymalfasin for HBV, HCV and certain cancers, as well as nearly 20 products in China, most of them partnered. 2Q11 SG&A was $21.1M, up 135% from $9M in 2Q10. The company attributed the increase to its April acquisition of Chinese pharmaceutical company NovaMed Pharmaceuticals Inc. The company confirmed its FY11 revenue guidance, excluding NovaMed, of $133-$138M.									
Simcere Pharmaceutical Group (NYSE:SCR)	$0.13	$0.21	Beat by $0.08	93%	$8.99	-$1.26	-12%	-$67.3	$480.5
2Q11 total revenues for the Chinese pharmaceutical company were RMB546.4M ($84.5M), up less than 1% from RMB544.6M in 2Q10, but below the Street's estimate of $89.4M. The company said revenue from certain branded generic products, including Zailin amoxicillin and Yingtaiqing diclofenac, fell by 8% to RMB205.3M ($31.7M) from RMB223.1M in 2Q10. Sales of cancer treatment Endu recombinant human endostatin rose 30% to RMB70 ($10.8M).									
WuXi PharmaTech Inc. (NYSE:WX)	$0.25	$0.25	Met	39%	$14.25	$0.23	2%	$16.3	$1,009.7
Earnings are per ADS. Total net revenue in 2Q11 was $101.1M, up 25% from $81M in 2Q10. The increase was driven by a 149% increase to $21M in manufacturing service sales. The R&D services company raised its net revenue guidance to $400-$407M from $390-$405M and provided 3Q11 revenue guidance of $100-$103M.									

Analyst picks & changes

Company	Bank	Analyst	Coverage	Opinion	Wk chg	8/12 cls
Charles River Laboratories International Inc. (NYSE:CRL)	Jefferies	David Windley	Price target	Hold	-6%	$30.84
Windley lowered his target to $33 from $40 after the tool supplier reported 2Q11 net sales from continuing operations of $288.3M, essentially flat vs. 2Q10. Windley believes the company's preclinical services (PCS) segment is stable but continues to hamper top-line growth. 2Q11 net sales for the PCS segment came in at $110.1M, down 9% from 2Q10 due to continued soft demand from large pharmas. Windley is cautious about the company's expectation that PCS sales will improve as pharma moves forward with facility closures and more extensive outsourcing.						
GTx Inc. (NASDAQ:GTXI)	Cowen	Eric Schmidt	Upgrade	Neutral (from underperform)	-11%	$2.97
Schmidt noted GTx's reduced valuation reflects the clinical and regulatory risks of its pipeline. He believes that Ostarine (GTx-024), a non-steroidal selective androgen receptor modulator (SARM) slated to start Phase III testing this quarter, "could have a role" in treating non-small cell lung cancer. Schmidt, however, thinks Capesaris (GTx-758) will prove inferior to Lupron Depot leuprolide from **Abbott Laboratories** (NYSE:ABT) on safety and/or efficacy in a Phase IIb trial to treat advanced prostate cancer. Data for the oral selective estrogen receptor alpha agonist are expected at year end.						
Human Genome Sciences Inc. (NASDAQ:HGSI)	Cowen	Eric Schmidt	Upgrade	Neutral (from underperform)	-1%	$15.68
Schmidt upgraded but lowered his worldwide peak sales estimate for Benlysta belimumab to $1.4B from $1.7B due to a "worrisome decline in projected future utilization" of the lupus drug based on his third survey of 32 U.S. lupus specialists. But while Schmidt continues to believe Benlysta sales will fall short of consensus expectations, he no longer views the stock as "substantially overvalued on a sum-of-the-parts basis." The human mAb against BLyS (B lymphocyte stimulator protein), partnered with **GlaxoSmithKline plc** (LSE:GSK; NYSE:GSK), is approved in the U.S., EU and Canada.						
MannKind Corp. (NASDAQ:MNKD)	JMP Securities	Jason Butler	Upgrade	Market outperform (from market perform)	4%	$2.79
Butler also set a $7 target after MannKind said that FDA confirmed the design of two additional Phase III trials of Afrezza in diabetes, requested by the agency in February *(see B19)*. He believes "the clinical risk for these trials is below average due to the extensive evidence of the drug's safety and efficacy demonstrated in previous trials." He anticipates the product will launch in 2014, with peak sales of $985M in 2020. Afrezza is a dry powder formulation of insulin plus an inhaler.						
PerkinElmer Inc. (NYSE:PKI)	Mizuho	Peter Lawson	Upgrade	Market outperform (from neutral)	0%	$22.53
Lawson upgraded based on the company's limited exposure to "higher risk" end markets, such as academia, pharma and government compared to its peers. He also sees significant margin upside and believes his estimate of low to mid organic growth for 2H11 is achievable for the instrument and reagents supplier.						
Regeneron Pharmaceuticals Inc. (NASDAQ:REGN)	Roth Capital Partners	Joseph Pantginis	Upgrade	Buy (from neutral)	16%	$54.18
Pantginis also raised his target to $65 from $60 ahead of anticipated FDA approval of a BLA for Eylea aflibercept ophthalmic solution (VEGF Trap-Eye) to treat wet age-related macular degeneration (AMD). The product, a human fusion protein that binds all forms of VEGF-A and placental growth factor (PIGF), has an Aug. 20 PDUFA date.						
Response Genetics Inc. (NASDAQ:RGDX)	Ladenburg Thalmann	Kevin DeGeeter	Downgrade	Neutral (from buy)	-11%	$2.12
DeGeeter downgraded based on four consecutive quarters of flat-to-down volume growth for the company's ResponseDx genetic tests and limited visibility on new products and a companion diagnostic strategy. He also thinks declining R&D investment over the past 4-5 quarters may be undercutting product development. Response Genetics markets PCR-based ResponseDX tests to diagnose lung, colon and gastric cancers and melanoma.						
Shire plc (LSE:SHP; NASDAQ:SHPGY)	UBS	Guillaume van Renterghem	Upgrade	Buy (from neutral)	3%	$95.67
van Renterghem also raised his target to 2,400p from 1,850p on the belief that the Street's 2013 EPS estimate is too low on "overly cautious" expectations for Shire's ADHD franchise. He expects the ADHD market will continue to grow, and Shire's ADHD drug Vyvanse lisdexamfetamine to have 18% of the market by 2013. He also expects sales of Shire's Adderall XR extended-release to remain around $450M with $70-$80M in royalties. Vyvanse is a prodrug of amphetamine, and Adderall XR is an extended-release formulation of Adderall, mixed salts of a single entity amphetamine.						
Theratechnologies Inc. (TSX:TH; NASDAQ:THER)	Bloom Burton	Philippa Flint	Upgrade	Hold (from sell)	9%	$3.99
Flint upgraded based on the recent selloff and the anticipated return to her target of C$4.50. In January, partner **Merck KGaA** (Xetra:MRK) launched Theratechnologies' Egrifta tesamorelin in the U.S. to treat HIV-infected patients with lipodystrophy. Egrifta is an analog of growth hormone releasing factor.						

BioCentury 100 Price & Volume Trend

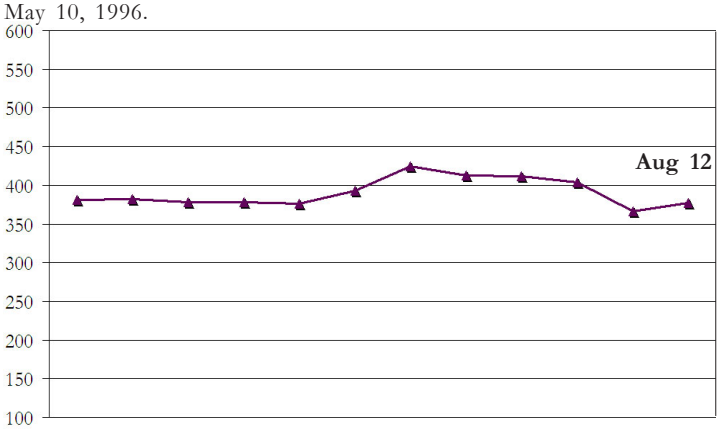
Cumulative weekly performance of 100 bioscience stocks. 12-week period. Line shows Price Level change (Left scale. Index base=1000 on May 10, 1996). Bars show cumulative volume in millions (right scale).



BioCentury tracks 577 issues that report prices and volume daily. The BioCentury 100 is a subset used to monitor price and volume trends.

BioCentury London Index

Weekly change in the combined market capitalization for 14 bioscience stocks listed on the LSE or AIM, 12-week period. Index base =1000 on May 10, 1996.



Price Gains

Stocks with greatest % price increase in the week ended Aug. 12.
(Priced above $2; 5,000 minimum share volume)

Company	Ticker	$Close	$Chg	%Chg	Vol(00)
Transition Therap[1]	TTHI	2.520	0.520	26%	6451
Cornerstone Therap	CRTX	8.260	1.330	19%	1755
Active Biotech	ACTI	SEK33.60	SEK5.40	19%	13777
Pharmasset	VRUS	125.030	18.540	17%	33392
Xoma	XOMA	2.000	0.290	17%	53990
Regeneron	REGN	54.180	7.370	16%	70632
Genmab	GEN	DKK42.44	DKK5.5	15%	6927
Devgen	DEVG	€5.560	€0.710	15%	3902
Progenics	PGNX	5.750	0.730	15%	9063
Amarin[2]	AMRN	12.870	1.630	15%	198841
Apricus Biosciences	APRI	4.270	0.520	14%	13114

Price Declines

Stocks with greatest % price decline (criteria as above).

Company	Ticker	$Close	$Chg	%Chg	Vol(00)
Oragenics	ORNI	2.050	-0.950	-32%	141
Idenix	IDIX	4.160	-1.680	-29%	75412
Amicus Therap	FOLD	4.300	-1.570	-27%	5492
Sagent Pharma	SGNT	20.000	-6.950	-26%	18127
D-Pharm	DPRM	NIS9.944	-NIS3.056	-24%	3427
BioLineRx[3]	BLRX	3.530	-0.970	-22%	11841
D. Western	4576	¥160.00	-¥42.00	-21%	54817
Osiris	OSIR	5.180	-1.350	-21%	10864
Kamada	KMDA	NIS18.90	-NIS4.92	-21%	2246
Protalix[4]	PLX	4.620	-1.050	-19%	30226

Volume Gains

Greatest changes in volume above 5,000 shares.

Company	Ticker	Vol(00)	%Chg	$Close	$Chg
Proximagen	PRX	1205	1360%	131p	1p
Sagent Pharma	SGNT	18127	699%	20.000	-6.950
PCI	PCIB	149	525%	NOK41.3	-NOK5.7
Newron	NWRN	1093	421%	CHF4.75	-CHF0.15
AcelRx	ACRX	353	410%	3.700	-0.310
Oragenics	ORNI	141	347%	2.050	-0.950
EpiStem	EHP	142	344%	380p	0p
Luminex	LMNX	50963	310%	22.040	2.360
Response Genetics	RGDX	885	256%	2.120	-0.270
Flamel	FLML	2848	215%	4.220	-0.230
Osiris	OSIR	10864	189%	5.180	-1.350
NeuroSearch	NEUR	3950	189%	DKK31.6	-DKK2.4

1 Includes volume from Toronto Stock Exchange
2 Volume figure is of ADSs (ADS = 1 share)
3 Includes volume from Tel Aviv Stock Exchange with ADSs converted (ADS = 10 shares)
4 Includes volume from Tel Aviv Stock Exchange

BioCentury 100 Advance-Decline Trend

Week ended	BC100 Price level	BC100 Stocks gaining	Gaining vol. (00)	BC100 Stocks declining	Declining vol. (00)
Jul 15	2528.60	33	1940683	66	3439789
Jul 22	2563.38	55	3362734	45	1868096
Jul 29	2426.47	11	949965	88	6085665
Aug 05	2120.01	1	72654	99	11089804
Aug 12	2130.98	47	4996600	53	6551978

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BioSante Pharmaceuticals Inc. (NASDAQ:BPAX)
Celldex Therapeutics Inc. (NASDAQ:CLDX)
Curis Inc. (NASDAQ:CRIS)
Dynavax Technologies Corp. (NASDAQ:DVAX)
ImmunoGen Inc. (NASDAQ:IMGN)
Map Pharmaceuticals Inc. (NASDAQ:MAPP)
Oncothyreon Inc. (NASDAQ:ONTY)
RaQualia Pharma Inc. (JASDAQ:4579)
Sangamo BioSciences Inc. (NASDAQ:SGMO)
Spectrum Pharmaceuticals Inc. (NASDAQ:SPPI)
SuperGen Inc. (NASDAQ:SUPG)
Targacept Inc. (NASDAQ:TRGT)
Ventrus Biosciences Inc. (NASDAQ:VTUS)
Vical Inc. (NASDAQ:VICL)
Ziopharm Oncology Inc. (NASDAQ:ZIOP)

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WEEK OF AUGUST 15, 2011

BioCentury

WEEK IN REVIEW (FORMERLY BIOCENTURY PART II)

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BioBusiness for the week ended August 12

COMPANY NEWS

Deals (Page B2)

Sales & Marketing (Page B5)

Using BioCentury Week in Review

You can read Week in Review online every Monday at www.biocentury.com

And you can set your own filters to customize your personal summary of the week's corporate, clinical and financial news.

BioCentury Week in Review (formerly BioCentury Part II) is a comprehensive compendium of business news for management and investors in bioscience companies. It is organized into three departments: Company News, Clinical News and Financial News.

The index on this page lists all the companies covered this week. The news items in each department are organized alphabetically by company. When more than one company is listed, the biotech company is shown first. Each brief is labeled with one or more applicable business categories from the following list:

ADMET; Agbio/Environmental; Antibodies; Autoimmune; Bioinformatics; Biomanufacturing; Biopharmaceuticals; Biosimilars; Cancer; Cardiovascular; Chemistry; Combinatorial biology; Computational chemistry/biology; Dental; Dermatology; Diagnostic; Drug delivery; Endocrine; Finance; Functional genomics; Gastrointestinal; Gene/Cell therapy; Generics; Genitourinary; Genomics; Hematology; Hepatic; High throughput screening; Infectious; Inflammation; Metabolic; Microarrays; Microfluidics; Musculoskeletal; Neurology; Nutraceuticals; Ophthalmic; Other; Pharmaceuticals; Pharmacogenetics; Proteomics; Pulmonary; Renal; Supply/Service; Transplant; Veterinary

Other News (Page B6)

Management Tracks (Page B8)

CLINICAL NEWS

Regulatory (Page B9)

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COMPANY NEWS/Deals, Sales & Marketing, Other News, Management Tracks

DEALS

Afexa Life Sciences Inc. (TSX:FXA), Edmonton, Alberta
Paladin Labs Inc. (TSX:PLB), Montreal, Quebec
Business: Nutraceuticals

Paladin began an unsolicited tender offer to acquire the 85.1% of Afexa it does not already own for either C$0.55 in cash or 0.013 Paladin shares. The offer values all of Afexa at C$56.8 million ($57.8 million) based on 103.2 million shares outstanding at June 24. It is a 15% premium to the company's close of C$0.48 on Aug. 9, before the offer was announced, and a 57% premium to Afexa's close of C$0.35 on July 14, before Paladin disclosed that it had acquired 5.4 million Afexa shares to bring its total stake in the nutraceutical company to 15.4 million shares, or about 14.9%. Paladin said the parties discussed strategic alternatives under an exclusivity agreement after it increased its stake in Afexa, but could not agree on terms for a deal by the Aug. 5 deadline. The tender offer expires Sept. 15 (*see BioCentury, July 25*).

Afexa's board said the offer "significantly undervalues" the company and advised shareholders to take no action at this time. The board said it would issue a formal position on the offer within the next 15 calendar days from Aug. 10. Scotia Capital is advising Afexa.

Affymax Inc. (NASDAQ:AFFY), Palo Alto, Calif.
Takeda Pharmaceutical Co. Ltd. (Tokyo:4502), Osaka, Japan
Business: Hematology

Affymax received a $10 million milestone payment from Takeda under an expanded 2006 deal to develop and commercialize peginesatide (formerly Hematide) to treat anemia. The milestone was triggered by FDA's acceptance in July of an NDA for the synthetic peptide-based erythropoiesis-stimulating agent (ESA) to treat anemia in chronic

See next page

Regulatory,
from previous page

(NASDAQ:BSTC)/Asahi Kasei
Chugai (Tokyo:4519)/Roche (SIX:ROG; OTCQX:RHHBY)
CombiMatrix (NASDAQ:CBMX)
Cumberland (NASDAQ:CPIX)
Cytori (NASDAQ:CYTX; Xetra:XMPA)
DiagnoCure (TSX:CUR)/Gen-Probe (NASDAQ:GPRO)
Eisai (Tokyo:4523; Osaka:4523)
Eisai (Tokyo:4523; Osaka:4523)/Novartis (NYSE:NVS; SIX:NOVN)
Endo (NASDAQ:ENDP)/Vernalis (LSE:VER)
Genentech/Boehringer Ingelheim/Roche (SIX:ROG; OTCQX:RHHBY)
Genentech/Teva (NASDAQ:TEVA)/Eli Lilly (NYSE:LLY)/Merck KGaA (Xetra:MRK)/Novartis (NYSE:NVS; SIX:NOVN)/Novo Nordisk (CSE:NVO; NYSE:NVO)/Pfizer (NYSE:PFE)/Roche (SIX:ROG; OTCQX:RHHBY)
Gilead (NASDAQ:GILD)/J&J (NYSE:JNJ)
InterMune (NASDAQ:ITMN)/Marnac/Shionogi (Tokyo:4507; Osaka:4507) Kamada (Tel Aviv:KMDA)
Neoprobe (NYSE:NEOP)
New York Blood Cntr
Qiagen (Xetra:QIA; NASDAQ:QGEN)
Quidel (NASDAQ:QDEL)
Salix (NASDAQ:SLXP)
Teva (NASDAQ:TEVA)
XenoPort (NASDAQ:XNPT)/Astellas (Tokyo: 4503)/ GlaxoSmithKline (LSE:GSK; NYSE:GSK)

Clinical Results (Page B13)

Adolor (NASDAQ:ADLR)/Eli Lilly (NYSE:LLY)
Biogen Idec (NASDAQ:BIIB)/Abbott (NYSE:ABT)
Eli Lilly (NYSE:LLY)
Genentech/Chugai (Tokyo:4519)/Roche (SIX:ROG; OTCQX:RHHBY)
Genentech/Roche (SIX:ROG; OTCQX:RHHBY)
Lexicon (NASDAQ:LXRX)
Oxford Bio (LSE:OXB)
Repros (NASDAQ:RPRX)
U of Pennsylvania

Preclinical Results (Page B15)

Arena (NASDAQ:ARNA)
CytRx (NASDAQ:CYTR)
iBio (NYSE-A:IBIO)
YM Bio (TSX:YM; NYSE-A:YMI)

Clinical Status (Page B16)

A.P. Pharma (OTCQB:APPA)
Amarin (NASDAQ:AMRN)
Anadys (NASDAQ:ANDS)
ArQule (NASDAQ:ARQL)/Daiichi Sankyo (Tokyo:4568; Osaka:4568)/Kyowa Hakko Kirin (Tokyo:4151)
AVI (NASDAQ:AVII)
Calando
Chelsea (NASDAQ:CHTP)/Dainippon Sumitomo (Tokyo:4506; Osaka:4506) Eisai (Tokyo: 4523; Osaka:4523)
Emergent (NYSE:EBS)
Exelixis (NASDAQ:EXEL)
Glenmark (NSE:GLENMARK; BSE:532296)
Immune Network (Pink:IMMFF)
Infinity (NASDAQ:INFI)
Infinity (NASDAQ:INFI)/Mundipharma
Inhibitex (NASDAQ:INHX)/Pfizer (NYSE:PFE)
Innate (Euronext:IPH)/Novo Nordisk (CSE:NVO; NYSE:NVO)
Isis (NASDAQ:ISIS)/OncoGenex (NASDAQ:OGXI)/Teva (NASDAQ:TEVA) MannKind (NASDAQ:MNKD)
Neovacs (Euronext:ALNEV)
Novavax (NASDAQ:NVAX)
Novo Nordisk (CSE:NVO; NYSE:NVO)
Orexo (SSE:ORX)
Pharming (Euronext:PHARM)
Portola/Novartis (NYSE:NVS; SIX:NOVN)
Progenics (NASDAQ:PGNX)/Salix (NASDAQ:SLXP)
Sygnis (Xetra:LIOK)
Synta (NASDAQ:SNTA)
Trius (NASDAQ:TSRX)/Dong-A (KSE:000640)/Bayer (Xetra:BAY)

FINANCIAL NEWS

Completed Offerings (Page B22)

Acutus
Agenus (NASDAQ:AGEN)
Enobia
IntelGenx (TSX-V:IGX; OTCBB:IGXT)
Jennerex
Knome
Microbix (TSX:MBX)
NeurogesX (NASDAQ:NGSX)
PharmaGap (TSX-V:GAP)
Second Genome
Sygnis Pharma AG (Xetra:LIOK), Heidelberg, Germany
T2 Biosystems
UgiChem
Verinata
Yaupon

Other Financial News (Page B22)

Affymax (NASDAQ:AFFY)
Cumberland (NASDAQ:CPIX)
Medifocus (TSX-V:MFS; OTCQX:MDFZF)
NPS (NASDAQ:NPSP)
Pharmasset (NASDAQ:VRUS)
Sigma-Aldrich (NASDAQ:SIAL)
Synta (NASDAQ:SNTA)
Technology Development Accelerator Fund
U of Oxford

Deals,
from previous page

kidney disease (CKD) patients on dialysis. The PDUFA date is March 27, 2012 (*see BioCentury, Feb. 20, 2006; July 3, 2006 & Aug. 1, 2011*).

Alere Inc. (NYSE:ALR), Waltham, Mass.
Axis-Shield plc (LSE:ASD; OSE:ASD), Dundee, U.K.
Business: Diagnostic

Alere began an unsolicited tender offer to acquire fellow diagnostics company Axis-Shield for 460p per share in cash. The price, which values Axis-Shield at about £230 million ($377.8 million), is a 37% premium to Axis-Shield's close of 335p on July 5, the day before Alere made the original offer. Axis-Shield said that it continues to believe the price undervalues the company. Axis-Shield added that it will provide a detailed response to shareholders no later than Aug. 25. The tender offer expires Sept. 1.

During the week, Alere said it increased its stake in Axis-Shield to 9.09% through open market purchases of 3.4 million shares. Shares were purchased at 444.75p-460p (*see BioCentury, Aug 8*).

Alere Inc. (NYSE:ALR), Waltham, Mass.
VitaPath Genetics Inc., Foster City, Calif.
Business: Diagnostic

Alere received exclusive, worldwide rights to develop and commercialize VitaPath's spina bifida risk assessment assay. Alere plans to launch the assay, which has completed a validation study, next year. The test is a pre-conception, multi-SNP, multi-gene, saliva based assay that predicts the risk of a child being born with spina bifida. Terms were not disclosed.

AMAG Pharmaceuticals Inc. (NASDAQ:AMAG), Lexington, Mass.
MSMB Capital Management LLC, New York, N.Y.
Business: Hematology

AMAG said its board unanimously rejected an unsolicited offer from shareholder MSMB Capital to acquire AMAG for $18 per share, or about $380.9 million in cash. AMAG said its board determined that MSMB's proposal "is not reasonably expected to result in a superior offer" to AMAG's planned merger with cancer company Allos Therapeutics Inc. (NASDAQ:ALTH, Westminster, Colo.). MSMB's proposed price is a 6% discount to AMAG's close of $19.07 on July 19, before AMAG agreed to merge with Allos (*see BioCentury, July 25 & Aug. 8*).

Amarantus BioSciences Inc. (OTCBB:AMBS), Sunnyvale, Calif.
Generex Biotechnology Corp. (OTCBB:GNBT), Toronto, Ontario
Business: Endocrine

The companies will use Amarantus' PhenoGuard cell immortalization process to develop beta cell replacement therapies to aid diabetes therapy. This is the third diabetes research collaboration between the companies *(see BioCentury, June 6 & July 18)*.

AnGes MG Inc. (Tokyo:4563), Osaka, Japan
GenoLac BL Corp., Okinawa, Japan
Business: Infectious

AnGes and GenoLac partnered to co-develop an HPV vaccine targeting E7 transforming protein (human papillomavirus-16; HpV16gp1). Details were not disclosed.

Array BioPharma Inc. (NASDAQ:ARRY), Boulder, Colo.
Roche (SIX:ROG; OTCQX:RHHBY), Basel, Switzerland
Business: Cancer

Array partnered with Roche's Genentech Inc. unit to develop each company's oral checkpoint kinase 1 (Chk1) inhibitor for cancer. Genentech will be responsible for all clinical development and commercialization. The deal includes Genentech's GDC-0425 (RG7602), which is in Phase 1 testing, and Array's ARRY-575, for which an IND will be submitted next quarter. Array will receive $28 million up front and is eligible for up to $685 million in total milestones for both compounds, plus double-digit royalties. Array will be eligible for a reduced amount in milestones if only one compound advances. Details were not disclosed.

Becton Dickinson and Co. (NYSE:BDX), Franklin Lakes, N.J.
Lab21 Ltd., Cambridge, U.K.
Business: Diagnostic

Becton Dickinson's BD Diagnostics unit and Lab21 partnered to develop a molecular diagnostic assay to detect *Aspergillus* fungus for use on BD's BD MAX Molecular Testing System. Lab21 will own IP resulting from the collaboration. Details were not disclosed.

biOasis Technologies Inc. (TSX-V:BTI), Vancouver, B.C.
Business: Neurology, Diagnostic

biOasis said its biOasis Advanced Technologies Inc. subsidiary acquired undisclosed IP from an undisclosed company for C$25,000 ($25,478) in cash, plus five-year warrants to purchase 350,000 shares at C$0.58 and 100,000 shares at C$0.50. If a patent associated with the IP is issued, the subsidiary will issue two-year warrants to purchase 300,000 shares. The warrants will be exercisable at the closing price on the date of issuance, but not less that C$0.50. biOasis' CogniTest, an Alzheimer's diagnostic melanoma-associated antigen p97 (MFI2; CD228) blood test, is being tested in human samples. The company is also developing Transcend, a p97 preclinical carrier protein that transports therapeutics across the blood brain barrier (BBB). Terms were not disclosed.

Bohai Pharmaceuticals Group Inc. (OTCBB:BOPH), Yantai, China
Yantai Tianzheng Pharmaceuticals Co. Ltd., Yantai, China
Business: Pharmaceuticals

Bohai acquired fellow traditional Chinese medicine company Yantai for $35 million in cash. Bohai said that Yantai's products complement and expand Bohai's portfolio. Yantai had 2010 revenue of $37.9 million. The company markets five herbal pharmaceuticals based on traditional Chinese medicines, including Fangfengtongsheng Granule to treat fever, headache, constipation, measles and eczema, and Zhengxintai Capsule to improve kidney function and treat coronary artery disease and angina. Bohai markets herbal medicines for rheumatoid arthritis (RA), viral infections, gynecological diseases, cardiovascular issues and respiratory diseases.

China Medical Technologies Inc. (NASDAQ:CMED), Beijing, China
Leica Microsystems GmbH, Wetzlar, Germany
Business: Diagnostic

Leica Microsystems' Biosystems division and China Medical will co-develop and commercialize automated fluorescence *in situ* hybridization (FISH) kits for tissue sample tests to detect EGFR, EGFR2 (HER2; ErbB2; neu) and topoisomerase II alpha (TOP2A) to be used on Leica Microsystems' BOND system. China Medical will sell the kits in China, and Leica will have an option to sell the kits in the rest of the world. Details were not disclosed.

Epixis S.A., Paris, France
Business: Infectious

Epixis said that an undisclosed U.S. biotech company has approached it with an acquisition offer. Epixis expects to disclose details next month. Epixis' hepatitis C virus-like particle (HCV-VLP) vaccine is in preclinical to treat and prevent HCV infection by inducing neutralizing antibodies.

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Deals,
from previous page

Evotec AG (Xetra:EVT), Hamburg, Germany
Business: Veterinary

Evotec granted an undisclosed animal health company exclusive, worldwide rights to EVT401 for veterinary uses. EVT401 is a small molecule P2X7 receptor antagonist. Evotec, which retains rights to the compound for human therapeutic uses, will receive an upfront payment and is eligible for milestones and tiered royalties. Evotec said EVT401 has completed Phase I testing, but the company has not chosen an indication to pursue. Details were not disclosed.

GATC Biotech AG, Konstanz, Germany
Sequenom Inc. (NASDAQ:SQNM), San Diego, Calif.
Business: Diagnostic

Sequenom granted GATC Biotech's LifeCodexx AG subsidiary European rights to patents covering the development of prenatal aneuploidy tests using fetal DNA in maternal plasma. Under the five-year deal, the partners will co-develop and commercialize a Trisomy 21 diagnostic test and other aneuploidy tests in Germany, Austria, Switzerland and Liechtenstein, with the potential for expansion into other countries. Sequenom will receive an upfront payment and is eligible for annual royalty payments, plus royalties on sales. Details were not disclosed.

Gilead Sciences Inc. (NASDAQ:GILD), Foster City, Calif.
Roche (SIX:ROG; OTCQX:RHHBY), Basel, Switzerland
Business: Cancer, Pulmonary

Gilead will acquire the Oceanside, Calif., biologics manufacturing facility of Roche's Genentech Inc. unit for an undisclosed amount. As part of the sale, Gilead will offer employment to about 55 Genentech employees. Gilead said it will use the facility for process development and manufacturing of GS 6624 (formerly AB0024) and another undisclosed preclinical antibody. Gilead acquired GS 6624 through its acquisition of Arresto BioSciences Inc. earlier this year. The humanized mAb against lysyl oxidase-like 2 (LOXL2) is in Phase I testing for idiopathic pulmonary fibrosis (IPF) and advanced solid tumors, and in Phase II for myelofibrosis. Gilead plans to begin Phase II testing of GS 6624 in colorectal and pancreatic cancer by year end. The deal is expected to close this quarter *(see BioCentury, Jan. 31)*.

Guided Therapeutics Inc. (OTCBB:GTHP), Norcross, Ga.
Konica Minolta Holdings Inc. (Tokyo:4902), Tokyo, Japan
Business: Diagnostic

Guided Therapeutics began a U.S. feasibility study under an amended 2010 deal with Konica Minolta's Konica Minolta Opto Inc. optics unit to use Guided Therapeutics' LightTouch technology to co-develop a product to detect and monitor Barrett's esophagus, a type of esophageal precancer. The study is evaluating Guided Therapeutics' light-based technology in about 40 patients and is expected to be completed by year end. In March, the parties extended the 2010 deal to 2012 *(see BioCentury, April 4)*.

A PMA application for Guided Therapeutics' LightTouch technology is under review. The point-of-care diagnostic analyzes wavelengths of light reflected from cervical tissue to detect cancerous and precancerous tissue.

Huya Bioscience International LLC, San Diego, Calif.
Shanghai Jiao Tong University, Shanghai, China
Business: Neurology

Huya received access and first review of therapeutics from the university's School of Pharmacy King's Lab, which is researching compounds to treat pain. The research laboratory will receive access to Huya's network of partners. Terms were not disclosed.

International Chemical Investors Group, Luxembourg, Luxembourg
Roche (SIX:ROG; OTCQX:RHHBY), Basel, Switzerland
Business: Supply/Service, Biomanufacturing

International Chemical will acquire Roche's Roche Colorado Corp. affiliate for an undisclosed sum. The facility, which includes a pharmaceutical production facility in Boulder, Colo., develops and manufactures peptides and small molecules. International Chemical plans to maintain operations at the Boulder location. The affiliate will be renamed Corden Pharma Colorado Inc. and will operate as part of International Chemical's Corden Pharma business. Under the deal, Corden Pharma Colorado will supply Roche with active pharmaceutical ingredients. The deal is expected to close this quarter.

Intercept Pharmaceuticals Inc., New York, N.Y.
Servier, Neuilly-sur-Seine, France
Business: Endocrine, Metabolic

The companies partnered to discover and develop treatments for Type II diabetes and other metabolic diseases from Intercept's G protein-coupled bile acid receptor 1 (GPBAR1; TGR5) agonist program. The partners will use Intercept's drug discovery technology, which is based on bile acid analog chemistry. Servier will have rights to the products outside of the U.S. and Japan, where Intercept retains rights.
Intercept could receive up to $163 million from the deal, including upfront, milestone and research payments. Intercept is also eligible for royalties. The partners will jointly support discovery, while Servier will be responsible for all costs associated with development and commercialization of selected lead candidates.

KV Pharmaceutical Co. (NYSE:KV-A), Bridgeton, Mo.
Zydus Cadila Group (NSE:CADILAHC; BSE:532321), Ahmedabad, India
Business: Generics

KV completed the divestiture of its Nesher Pharmaceuticals Inc. generics subsidiary to Zydus Cadila's Zydus Pharmaceuticals USA Inc. subsidiary for $60 million in cash (*see BioCentury, June 20*).

Isis Pharmaceuticals Inc. (NASDAQ:ISIS), Carlsbad, Calif.
CHDI Foundation Inc., New York, N.Y.
Business: Neurology

Not-for-profit foundation CHDI and Isis renewed a 2007 deal to discover and develop an antisense treatment for Huntington's disease (HD). CHDI will provide Isis with funding to identify and conduct preclinical testing on an antisense candidate. The renewal also provides Isis with up to $2 million in funding to cover HD research expenses incurred since the three-year agreement ended in 2010. The companies will continue to collaborate after IND-enabling studies. Details were not disclosed (*see BioCentury, Nov. 5, 2007*).

ProBioGen AG, Berlin, Germany
Boehringer Ingelheim GmbH, Ingelheim, Germany
Business: Antibodies

Boehringer received a non-exclusive license to use ProBioGen's GlymaxX technology to enhance antibody-dependent cellular cytotoxicity (ADCC) activity of antibodies. Boehringer said its contract manufacturing business will use the technology in its high expression Chinese hamster ovary (CHO)-based Bi-HEX system. The partners agreed to jointly market the technology and offer it to customers royalty-free. Financial details were not disclosed.

Sequenom Inc. (NASDAQ:SGNM), San Diego, Calif.
TrovaGene Inc. (Pink:TROV), San Diego, Calif.
Business: Diagnostic

TrovaGene (formerly Xenomics Inc.) said a 2008 deal that gave

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Deals,
from previous page

Sequenom rights to TrovaGene's transrenal technology was terminated. TrovaGene regains rights to patents covering transrenal fetal nucleic acids found in maternal urine for noninvasive prenatal and cancer diagnostics. Sequenom said it returned the rights because it could not make commercial use of the technology. TrovaGene added that it is in partnering discussions for the technology. Details were not disclosed.

Last year, the U.S. District Court for the Southern District of New York dismissed a suit from TrovaGene seeking to recover the technology, plus damages. However, Sequenom said the companies never began the arbitration process. The court said the companies must settle the dispute via arbitration, as stipulated by the original deal. TrovaGene had alleged that Sequenom manipulated data for its SEQureDx Down syndrome test to induce Xenomics into the deal. Sequenom subsequently retracted the data and delayed the test due to employee mishandling (*see BioCentury, Nov. 3, 2008 & Dec. 21, 2009*).

ShangPharma Corp. (NYSE:SHP), Shanghai, China
Business: Cancer

ShangPharma said it received an undisclosed milestone payment from an undisclosed U.S. pharmaceutical company. The milestone was triggered by advancing two clinical cancer programs to the next stage of development. Terms were not disclosed. ShangPharma provides R&D services to biotech and pharma companies.

Via Science Inc., Cambridge, Mass.
Bristol-Myers Squibb Co. (NYSE:BMY), New York, N.Y.
Business: Inflammation, Autoimmune

Via's GNS Healthcare Inc. healthcare analytics subsidiary and Bristol-Myers partnered to discover disease biology and biomarkers in the area of immuno-inflammation diseases. Bristol-Myers will provide genetic, molecular and clinical outcome data from an undisclosed clinical trial. GNS will identify molecular mechanisms and potential drug targets using its REFS platform to construct an inflammation disease model intended to support virtual clinical trials that will simulate the clinical effect of inhibiting specific targets. GNS said that the model may enable development of novel therapies for specific genetic and phenotypes to optimize individualized patient outcomes. Details were not disclosed.

Unigene Laboratories Inc. (OTCBB:UGNE), Boonton, N.J.
GlaxoSmithKline plc (LSE:GSK; NYSE:GSK), London, U.K.
Business: Musculoskeletal

Unigene and GlaxoSmithKline signed a separate deal under which Unigene will conduct development and manufacturing activities related to the active pharmaceutical ingredient and finished drug product for its oral parathyroid hormone (PTH). Unigene will be eligible for about $2.2 million in milestones. Under a 2002 deal that was amended in 2010, GSK has an option to assume responsibility for all future development and commercialization of the PTH analog after Unigene completes a Phase II trial to treat osteoporosis in postmenopausal women. Data from the trial are expected by the end of the year, after which GSK will have 75 days to exercise its option. If the pharma exercises its option, Unigene will be eligible for about $140 million in milestones, plus tiered, double-digit royalties in the mid to low teens (*see BioCentury, April 22, 2002 & Dec. 20, 2010*).

SALES & MARKETING

Abbott Laboratories (NYSE:ABT), Abbott Park, Ill.
Business: Infectious

Abbott's Ibis Biosciences Inc. subsidiary launched its PLEX-ID test to detect vector-borne microorganisms. The molecular assay, which uses PCR and mass spectrometry to characterize known and unknown organisms, is not intended for use in diagnostics.

Affymetrix Inc. (NASDAQ:AFFX), Santa Clara, Calif.
Business: Microarrays

Affymetrix launched its GeneChip Human Transcriptome and Splice Junction Array worldwide for research use. The array is available through an early access program to pharmaceutical and research institutions using microarrays or next-generation sequencing for basic discovery or whole transcriptome analysis. Affymetrix expects the array for high throughput clinical trials to be fully commercialized with integrated software early next year.

Astellas Pharma Inc. (Tokyo:4503), Tokyo, Japan
Teijin Pharma Ltd., Tokyo, Japan
Business: Metabolic

Teijin granted Astellas exclusive rights to market Feburic febuxostat in Thailand, the Philippines, Indonesia, Singapore, Malaysia, Vietnam and India. Astellas will be responsible for gaining regulatory approval of the non-purine selective inhibitor of xanthine oxidase in the territories, where sales are expected to commence in 2015. Teijin launched the product to treat hyperuricemia in Japan in May and in Korea in July. Takeda Pharmaceutical Co. Ltd. (Tokyo:4502, Osaka, Japan) markets febuxostat as Uloric in the U.S., where it has rights from Teijin. Terms were not disclosed *(see BioCentury, Aug. 8)*.

Baxter International Inc. (NYSE:BAX), Deerfield, Ill.
Halozyme Therapeutics Inc. (NASDAQ:HALO), San Diego, Calif.
Business: Endocrine

Halozyme disclosed in its 1H11 earnings that Baxter transferred to it certain marketing rights and assets related to Hylenex recombinant human PH20 hyaluronidase enzyme. The companies have also entered into a supply agreement, under which Baxter will provide Hylenex fill-finish services until Halozyme transfers to a new manufacturing site. Financial terms were not disclosed.

Baxter, which markets Hylenex in the U.S. to increase absorption and dispersion of other injected drugs, has exclusive, worldwide rights to market and distribute Hylenex under an expanded 2004 deal. Last year, Halozyme and Baxter recalled all manufactured lots of Hylenex after flake-like particles, identified as glass, were observed in vials of the product during stability testing. Halozyme expects the reintroduction of Hylenex by year end *(see BioCentury, May 24, 2010 & Sept. 6, 2010)*.

Cepheid Inc. (NASDAQ:CPHD), Sunnyvale, Calif.
Business: Diagnostic

Cepheid launched its updated Xpert BCR-ABL Monitor test in Europe to monitor the BCR-ABLE gene transcript in peripheral blood specimens from Philadelphia chromosome-positive chronic myelogenous leukemia (Ph+ CML) patients. The test, which has CE Mark approval, was updated to incorporate a fully validated test-specific conversion factor aligned to the International Scale.

Novartis AG (NYSE:NVS; SIX:NOVN, Basel, Switzerland) has exclusive development and commercialization rights to the RT-PCR assay in the U.S. to monitor patients for minimal residual disease and to identify patients with high risk for relapse from a 2010 deal. Novartis markets CML drug Gleevec imatinib *(see BioCentury, Oct. 18, 2010)*.

Enigma Diagnostics Ltd., Salisbury, U.K.
GlaxoSmithKline plc (LSE:GSK; NYSE:GSK), London, U.K.
Business: Diagnostic

Enigma granted GlaxoSmithKline exclusive rights to commercialize

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Sales and Marketing,
from previous page

Enigma's Enigma Mini Laboratory (ML) real-time PCR technology for point-of-care diagnostics in respiratory indications in Europe and other countries, including India, Brazil and Russia. Enigma plans to begin commercialization of the Enigma ML system next year. GlaxoSmithKline will make an undisclosed equity investment in Enigma. Enigma will also receive an undisclosed upfront payment and R&D funding, and is eligible for milestones and royalties. The collaboration is an extension of a 2009 deal, in which the companies partnered to develop and commercialize a diagnostic to identify influenza strains using Enigma ML. Details were not disclosed *(see BioCentury, July 27, 2009)*.

Hope Pharmaceuticals Inc., Scottsdale, Ariz.
Business: Other

Hope launched Nithiodote sodium nitrate/sodium thiosulfate injection in the U.S. to treat acute cyanide poisoning. Terms were not disclosed.

Meridian Bioscience Inc. (NASDAQ:VIVO), Cincinnati, Ohio
Business: Diagnostic

Meridian launched its ImmunoCard C. difficile test in Europe to detect *Clostridium difficile* infection (CDI). The assay detects glutamate dehydrogenase in stool samples.

NanoString Technologies Inc., Seattle, Wash.
Business: Functional genomics

NanoString launched its nCounter Rat miRNA Expression Assay Kit worldwide to perform direct digital detection and counting of tissue-specific microRNAs at single-base resolution for research use only. The test runs on NanoString's fully automated detection and counting system nCounter Analysis System.

Northwest Biotherapeutics Inc. (OTCBB:NWBO), Bethesda, Md.
Business: Cancer

Northwest said its DCVax immunotherapies would be priced in the range of $37,000 per year for up to three years of treatment. The announcement came in response to investors' concerns over pricing and reimbursement of prostate cancer drug Provenge sipuleucel-T from Dendreon Corp. (NASDAQ:DNDN, Seattle, Wash.). Earlier this month, Dendreon said it expects to cut expenses to account for reduced near-term manufacturing needs after the company withdrew its full year revenue guidance as a result of lower-than-expected uptake of the prostate cancer therapy. A full-course of three doses of Provenge costs $93,000. Northwest expects to start Phase III testing as early as 1Q12 for its prostate cancer candidate DCVax-Prostate. DCVax-Prostate consists of autologous dendritic cells treated *ex vivo* with prostate-specific membrane antigen (PSMA) (*see BioCentury, Aug. 8*).

Nycomed, Zurich, Switzerland
Orion Corp. (HSE:ORNAV; HSE:ORNBV), Espoo, Finland
Business: Drug delivery, Inflammation, Pulmonary

The companies partnered to co-market Easyhaler combination products being developed by Orion for the treatment of asthma and chronic obstructive pulmonary disease (COPD) in European countries, including Austria, the Benelux countries, France, Germany, Greece, Italy, Poland, Portugal, Spain and Switzerland. Orion will retain marketing rights in the Nordic countries, U.K. and Eastern Europe and will exclusively manufacture all products under the deal. Nycomed also received an exclusive license to market Easyhaler products in the Middle East and North African region. Details were not disclosed.

Orion markets several dry-powder formulations of asthma and COPD generic drugs for use with the Easyhaler inhaler, which had 2010 sales of €28 million ($37.4 million).

Progenics Pharmaceuticals Inc. (NASDAQ:PGNX), Tarrytown, N.Y.
Salix Pharmaceuticals Ltd. (NASDAQ:SLXP), Morrisville, N.C.
Business: Gastrointestinal

Progenics disclosed in its 2Q11 earnings conference call that Salix has secured a commercialization deal for Relistor methylnaltrexone in Australia and some related Asian territories. Additionally, Progenics said an EU partnership is expected to close by Oct. 1. The subcutaneous formulation of the peripheral mu opioid receptor antagonist is approved in more than 50 countries, including the U.S. and those of the EU, to treat OIC in patients receiving palliative care. Salix has exclusive, worldwide rights from Progenics to develop and commercialize all formulations of Relistor, excluding Japan, where Ono Pharmaceutical Co. Ltd. (Tokyo:4528; Osaka:4528, Osaka, Japan) has rights to the subcutaneous formulation. Progenics reported 2010 worldwide Relistor net sales of $16.1 million (*see BioCentury, Feb. 14*).

Response Genetics Inc. (NASDAQ:RGDX), Los Angeles, Calif.
Business: Diagnostic

Response Genetics disclosed in its 2Q11 earnings that it launched its ResponseDx: Melanoma in the U.S. to detect BRAF mutations to assess treatment for skin cancer patients.

Sequenom Inc. (NASDAQ:SQNM), San Diego, Calif.
Business: Diagnostic

Sequenom disclosed in its 1H11 earnings that it launched RetnaGene AMD test in the U.S. to assess the risk of developing wet age-related macular degeneration (AMD). The test, which became available May, provides a patient risk score based on 13 genetic markers associated with the disease.

OTHER NEWS

Boehringer Ingelheim GmbH, Ingelheim, Germany
Business: Infectious

Boehringer will extend and expand price reduction and rebate programs for its HIV drugs to AIDS Drug Assistance Programs (ADAPs). The agreement with the ADAP Crisis Task Force (ACTF) extends rebates mandated by health reform through 2013 and extends price freezes on HIV drugs purchased by ADAPs. Boehringer markets HIV drugs Aptivus tipranavir, Viramune nevirapine and Viramune XR, an extended release form of Viramune. Aptivus is a non-peptidic protease inhibitor (PI), while Viramune is non-nucleoside reverse transcriptase inhibitor (NNRTI).

Caliper Life Sciences Inc. (NASDAQ:CALP), Hopkinton, Mass.
Carestream Health Inc., Rochester, N.Y.
Stanford University, Stanford, Calif.
Business: Other

Caliper and Carestream settled two lawsuits related to their respective imaging systems. Under the settlement, the companies will dismiss their respective suits and Carestream will not market *in vivo* optical imaging systems for applications covered by patents Caliper and its Xenogen Corp. subsidiary licensed from the university. Carestream also agreed not to assert that Caliper's IVIS Lumina XR imaging system infringes any of Carestream's patents. IVIS Lumina XR combines florescence, bioluminescence and X-ray imaging capabilities to image animals in preclinical testing.

In February 2010, Caliper, Xenogen and the university filed suit in the U.S. District Court for the Northern District of California alleging

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that Carestream's marketing of its instrument systems infringed seven patents covering non-invasive *in vivo* imaging of fluorescence and bioluminescence in animals. In July 2010, Carestream filed suit against Caliper in the U.S. District Court for the Western District of Wisconsin alleging that Calipers' IVIS Lumina XR imaging system infringes Carestream's U.S. Patent No. 7,734,325 covering an apparatus and methods for imaging a small animal using X-ray, radioisotopic, fluorescence and luminescence modalities without moving the animal (*see BioCentury, July 19, 2010*).

Epigenomics AG (Xetra:ECX), Berlin, Germany
Business: Genomics, Diagnostic

Epigenomics will restructure and reduce headcount by about 39 (46%) to 45 and will discontinue early stage research to focus on the U.S. market. Details on the cuts were not disclosed. Epigenomics said it is preparing for the U.S. launch of its second-generation colorectal cancer test Epi proColon 2.0, for which a PMA submission is slated next quarter.

A first-generation version of the test is approved in Europe, but Epigenomics said uptake has been slower than expected. As a result, the company plans to focus on private and public health plans and screening organizations rather than primary care physicians and self-payers. However, Epigenomics does plan to launch the second-generation version in Europe by year end. Additionally, the company said it will scale down clinical research, including its PITX2 gene methylation assay to detect the risk of prostate cancer recurrence. The company said it is in discussions with several parties to out-license the assay. Epigenomics also plans to relocate its U.S. headquarters from Seattle to the East Coast in 2012. The changes are expected to save about €3.5-€4 million ($5-$5.7 million) annually. At June 30, the company had €20.7 million ($29.7 million) in cash and a six-month net loss of €5.9 million ($8.5 million).

Forest Laboratories Inc. (NYSE:FRX), New York, N.Y.
Business: Generics, Pharmaceuticals

Forest and activist investor Carl Icahn issued dueling SEC filings last week arguing in favor of their respective director slates ahead of the company's Aug. 18 annual meeting. Icahn said his proposed slate of four directors — Alexander Denner, Richard Mulligan, Lucian Bebchuck and Eric Ende — would help Forest address upcoming challenges such as patent expirations for antidepressant Lexapro escitalopram and Alzheimer's disease (AD) drug Namenda memantine. Lexapro comes off patent in March 2012 and Namenda comes off patent in April 2015.

Forest reiterated concerns about potential conflicts of interest for Denner and Mulligan, who both serve on the boards of Biogen Idec Inc. (NASDAQ:BIIB, Weston, Mass.) and Enzon Pharmaceuticals Inc. (NASDAQ:ENZN, Bridgewater, N.J.). Denner also is a director at Amylin Pharmaceuticals Inc. (NASDAQ:AMLN, San Diego, Calif.). Forest proposed its own slate of candidates last month. Icahn and his affiliates held a 9.2% stake in Forest at Aug. 10 *(see BioCentury, June 20; July 4 & July 25)*.

Gilead Sciences Inc. (NASDAQ:GILD), Foster City, Calif.
Astellas Pharma Inc. (Tokyo:4503), Tokyo, Japan
Business: Infectious

Gilead said FDA accepted the company's response to a warning letter issued last year over violations of cGMP regulations identified during an inspection of the company's San Dimas, Calif., manufacturing facility. Gilead said the issues were primarily related to the manufacturing environment for antifungal drug AmBisome liposomal amphotericin B. At the time, Gilead said the letter could impact the company's ability to supply AmBisome, cystic fibrosis drug Cayston aztreonam lysine and ophthalmic drug Macugen pegaptanib (*see BioCentury, Oct. 4, 2010*).

Pfizer Inc. (NYSE:PFE, New York, N.Y.) markets Macugen outside the U.S., where Eyetech has rights from OSI Pharmaceuticals Inc., now part of Astellas. In 2005, OSI acquired Eyetech Pharmaceuticals Inc., which developed the pegylated aptamer that binds to VEGF 165 and uses technology licensed from Gilead, and spun the company out in 2008 as Eyetech Inc. (Palm Beach Gardens, Fla.). AmBisome is partnered with Astellas.

H. Lundbeck A/S (CSE:LUN), Copenhagen, Denmark
Business: Neurology

H. Lundbeck announced in its 1H11 earnings statement that it will reduce headcount by 125-175 (2-3%) as part of its optimization program. The pharma said it has about 5,900 employees. The cuts, which are expected primarily in Denmark and the U.S., will be from R&D but Lundbeck said it will not result in any major changes to its general R&D approach. At June 30, Lundbeck had DKK2.9 billion ($562.5 million) in cash and a six-month operating profit of DKK2.4 billion ($467.7 million). Details were not disclosed.

Johnson & Johnson (NYSE:JNJ), New Brunswick, N.J.
Business: Neurology

Johnson & Johnson disclosed in its 2Q11 earnings that an agreement in principal has been reached on key issues relevant to a misdemeanor criminal charge related to the promotion of antipsychotic Risperdal risperidone, but certain issues remain open before a settlement can be finalized. The U.S. Department of Justice and the U.S. Attorney's Office for the Eastern District of Pennsylvania are pursing criminal and civil actions concerning sales and marketing of Risperdal, including for off-label uses. The company could not be reached for comment.

In June, Circuit Court Judge Roger Couch awarded the state of South Carolina civil penalties totaling $327 million following a March verdict in which a jury ruled that the J&J's Ortho-McNeil-Janssen Pharmaceuticals Inc. unit willfully violated the South Carolina Unfair Trade Practices Act. The jury found that the pharma engaged in unfair or deceptive acts or practices in the conduct of any trade or commerce for Risperdal. J&J reported 1H11 U.S. sales of $19 million for Risperdal *(see BioCentury, June 13)*.

Merck & Co. Inc. (NYSE:MRK), Whitehouse Station, N.J.
Business: Cancer, Infectious

Merck received a subpoena from the U.S. Department of Justice regarding the marketing of cancer drug Temodar temozolomide, HCV drug PegIntron peginterferon alfa-2b and cancer and viral infection drug Intron A interferon alfa-2b between 2004 and the present. Merck is cooperating with the investigation. At June 30, six-month sales for Temodar, PegIntron and Intron A were $481 million, $319 million and $96 million, respectively. Details were not disclosed.

Separately, Merck closed its small interfering RNA research facility in San Francisco, Calif., and released about 45 scientists, while about five scientists were offered positions in the pharma's facility in West Point, Pa. Merck said it will continue to invest significantly in siRNA research. Merck gained the facility through its 2006 acquisition of Sirna Therapeutics Inc. (*see BioCentury, Jan. 8, 2007*).

Orexigen Therapeutics Inc. (NASDAQ:OREX), La Jolla, Calif.
Business: Endocrine

Orexigen disclosed in its 2Q11 earnings that it reduced headcount by an undisclosed number as part of the suspension of all of its obesity programs announced in June. The move follows the failure of Orexigen's

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appeal of FDA's request for a larger-than-expected cardiovascular outcomes trial of obesity candidate Contrave. Orexigen and the agency were unable to come to an agreement on the trial design. In February, Orexigen reduced headcount by 23 (40%) to save cash after FDA issued a complete response letter for Contrave. In the letter, the agency requested the company run a larger-than-expected cardiovascular outcomes trial prior to approval to show that the risk of major adverse cardiovascular events in patients receiving Contrave does not adversely affect the drug's benefit-risk profile.

The current cuts are expected to substantially lower costs in 2H11 over 1H11. At June 30, Orexigen had $69.7 million in cash and a six-month operating loss of $19 million. Contrave is a fixed-dose combination of naltrexone HCL sustained release (SR) and bupropion HCL SR *(see BioCentury, June 6)*.

Osteologix Holdings plc (Pink:OLGXF), Bray, Ireland
Business: Musculoskeletal

Osteologix completed the consolidation of its operations in Ireland. Parent company Osteologix Inc. has been dissolved and former shareholders received shares of Osteologix Holdings. All operations in Virginia have ceased. The company said it is seeking to minimize overhead expenses, while focusing on its NB S101 licensing agreement with Servier (Neuilly-sur-Seine, France) and continuing to seek U.S. development partners for the compound. Last year, Osteologix granted Servier exclusive, ex-U.S. rights to develop and commercialize NB S101 to treat postmenopausal osteoporosis, other bone and joint disorders, and dental indications. The strontium formulation has completed Phase II testing to treat osteoporosis and is in preclinical testing to treat osteoarthritis and osteonecrosis. At Sept. 30, 2010, Osteologix Inc. reported $4.1 million in cash and a nine-month operating loss of $836,000 *(see BioCentury, Aug. 9, 2010 & Dec. 20, 2010)*.

Pfizer Inc. (NYSE:PFE), New York, N.Y.
University of California, San Diego, Calif.
Business: Pharmaceuticals

The university joined Pfizer's Global Centers for Therapeutic Innovation initiative. The pharma launched the initiative last year to establish partnerships with academic medical centers for drug discovery and development. Under the initiative, Pfizer will provide its partners with funding for preclinical and clinical development programs, as well as offer IP and ownership rights, in return for options to license exclusive rights to drug candidates. The university said the value could exceed $50 million over the next five years. The university will also have will have access to some of Pfizer's antibody libraries and technologies, and will be eligible for milestones and royalties on mutually agreed-upon drug candidates *(see BioCentury, Nov. 22, 2010, Jan. 31, 2011 & June 13, 2011)*.

Pozen Inc. (NASDAQ:POZN), Chapel Hill, N.C.
Dr. Reddy's Laboratories Ltd. (NYSE:RDY), Hyderabad, India
Mylan Inc. (NASDAQ:MYL), Canonsburg, Pa.
Par Pharmaceutical Cos. Inc. (NYSE:PRX), Woodcliff Lake, N.J.
Business: Neurology

A judge in the U.S. District Court for the Eastern District of Texas ruled that Pozen's U.S. Patent Nos. 6,060,499; 6,586,458; and 7,332,183 covering migraine drug Treximet sumatriptan/naproxen are valid and enforceable. The court ruling precluded FDA from approving an ANDA for a generic version of the combination of sumatriptan and naproxen sodium from Mylan's Alphapharm Pty. Ltd. generics subsidiary prior to the expiration of the '499 and '458 patents in August 2017. Additionally, FDA cannot approve ANDAs from Par and Dr. Reddy's until the expiration of the '183 patent in February 2025. The '183 patent was not asserted against Alphapharm. GlaxoSmithKline plc (LSE:GSK; NYSE:GSK, London, U.K.) has U.S. marketing rights to Treximet from Pozen under a 2003 deal. GSK reported 2010 Treximet sales of £56 million ($86.7 million) *(see BioCentury, March 28 & April 25)*.

Teva Pharmaceutical Industries Ltd. (NASDAQ:TEVA), Petah Tikva, Israel
GlaxoSmithKline plc (LSE:GSK; NYSE:GSK), London, U.K.
Pfizer Inc. (NYSE:PFE), New York, N.Y.
Business: Infectious

ViiV Healthcare LLC, a JV between GlaxoSmithKline and Pfizer, filed suit in the U.S. District Court for the District of Delaware against Teva alleging that an ANDA filed for a generic version of HIV drug Epzicom abacavir/lamivudine infringes U.S. Patents No. 6,417,191 covering combinations of abacavir and lamivudine. The ANDA filing contained a Paragraph IV certification claiming that the patent is invalid and/or unenforceable, and that the claims in the '191 patent would not be infringed by the ANDA. The patent expires in March 2016.

ViiV markets GSK's Epzicom, an oral fixed-dose combination of nucleoside reverse transcriptase inhibitors lamivudine and abacavir. GSK reported 1H11 worldwide and U.S. sales of £287 million ($461.5 million) and £104 million ($167.2 million) for Epzicom, respectively.

MANAGEMENT TRACKS

Boards of Directors

PLx Pharma Inc., Houston, Texas
Business: Autoimmune, Neurology
Appointed: Michael Valentino as chairman, formerly president and CEO of Xanodyne Pharmaceuticals Inc.

T2 Biosystems Inc., Lexington, Mass.
Business: Diagnostic
Appointed: Josh Bilenker, principal at Aisling Capital

Management

Acucela Inc., Seattle, Wash.
Business: Ophthalmic
Hired: Michelle Carpenter as SVP of regulatory affairs and development operations, formerly executive director of regulatory affairs of Dow Pharmaceutical Sciences Inc., which was acquired by Valeant Pharmaceuticals International Inc.

Arena Pharmaceuticals Inc. (NASDAQ:ARNA), San Diego, Calif.
Business: Endocrine, Neurology, Cardiovascular
Hired: Robert Hoffman as VP of finance and CFO after departing as CFO of Polaris Pharmaceuticals Inc.

Auxilium Pharmaceuticals Inc. (NASDAQ:AUXL), Malvern, Pa.
Business: Endocrine, Genitourinary
Promoted: James Tursi to CMO from VP of clinical R&D

Avanir Pharmaceuticals Inc. (NASDAQ:AVNR), Aliso Viejo, Calif.
Business: Neurology, Infectious, Inflammation
Hired: Joao Siffert as SVP of R&D, a newly created position, formerly VP and CMO of Ceregene Inc.

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CLINICAL NEWS

Clinical activities and selected announcements for the week ended August 12.

REGULATORY

Adventrx Pharmaceuticals Inc. (NYSE-A:ANX), San Diego, Calif.
Product: Exelbine vinorelbine emulsion (ANX-530)
Business: Cancer

Adventrx received a complete response letter from FDA for an NDA for Exelbine vinorelbine injectable emulsion to treat non-small cell lung cancer (NSCLC). According to the company, FDA said the authenticity of the drug products used in Adventrx's bioequivalence trial could not be verified following inspections at clinical sites. The agency said the trial will need to be repeated to address the deficiency. Adventrx said it believes the procedures used in the trial were adequate to verify the authenticity of the products. The company plans to request a meeting with the agency this week.

Adventrx resubmitted the NDA last November with 12 months of site-specific stability data after the agency refused to file the application in March, citing insufficiencies in the CMC section *(see BioCentury, March 8, 2010 & Nov. 8, 2010)*. The NDA for the anti-mitotic chemotherapeutic agent was submitted under section 505(b)(2) of the Food, Drug and Cosmetic Act, which allows sponsors to reference data on safety and efficacy from the scientific literature or from previously approved products. Exelbine is an emulsion formulation of vinorelbine tartrate, an anti-mitotic chemotherapeutic agent.

Affymax Inc. (NASDAQ:AFFY), Palo Alto, Calif.
Takeda Pharmaceutical Co. Ltd. (Tokyo:4502), Osaka, Japan
Product: Peginesatide (formerly Hematide)
Business: Hematology

Affymax said FDA assigned a PDUFA date of March 27, 2012, for an NDA for peginesatide to treat anemia in chronic kidney disease (CKD) patients on dialysis. Takeda and Affymax will co-commercialize the synthetic peptide-based erythropoiesis-stimulating agent (ESA) in the U.S., while Takeda has exclusive rights elsewhere.

Alkermes Inc. (NASDAQ:ALKS), Waltham, Mass.
Amylin Pharmaceuticals Inc. (NASDAQ:AMLN), San Diego, Calif.
Eli Lilly and Co. (NYSE:LLY), Indianapolis, Ind.
Product: Bydureon exenatide once weekly
Business: Endocrine

FDA accepted an NDA resubmission from Amylin for Type II diabetes candidate once-weekly Bydureon exenatide. The agency designated the NDA a Class 2 resubmission, with a PDUFA date of Jan. 28, 2012. The resubmission includes results from a thorough QT study released last month showing no significant corrected QT interval prolongation associated with the long-acting release (LAR) formulation of synthetic exendin-4. FDA asked for the tQT study in a complete response letter issued last October *(see BioCentury, July 11)*. Amylin and Eli Lilly developed Bydureon, which uses drug delivery technology from Alkermes.

Allergan Inc. (NYSE:AGN), Irvine, Calif.
GlaxoSmithKline plc (LSE:GSK; NYSE:GSK), London, U.K.
Product: Botox onabotulinumtoxinA (formerly botulinum toxin)
Business: Genitourinary

Allergan said the Irish Medicines Board issued a positive opinion for the approval of Botox in 14 EU member states to manage urinary incontinence in adults with neurogenic detrusor overactivity resulting from neurogenic bladder due to stable sub-cervical spinal cord injury (SCI) or multiple sclerosis (MS). The application was submitted under the EU Mutual Recognition Procedure, with Ireland acting as the reference member state. The vacuum-dried purified botulinum toxin type A is approved in the U.K. in adults to treat severe axillary hyperhidrosis (excessive sweating) of the armpits, cervical dystonia,

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Management Tracks,
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CytomX Therapeutics Inc., South San Francisco, Calif.
Business: Antibodies
Transitioned: Sean McCarthy to CEO from CBO; he succeeds co-founder Nancy Stagliano, who will join the company's scientific advisory board

Exagen Diagnostics Inc., Albuquerque, N.M.
Business: Diagnostic
Hired: Eric Tornoe as president and COO, formerly head of Enbrel etanercept global marketing at Pfizer Inc.

Human Genome Sciences Inc. (NASDAQ:HGSI), Rockville, Md.
Business: Cancer, Infectious, Autoimmune
Hired: Craig Parker as SVP of strategy and corporate development, formerly CEO and co-founder of Vega Therapeutics Inc.

Nanospectra Biosciences Inc., Houston, Texas
Business: Cancer
Hired: John Stroh as president, CEO and a director, formerly interim CEO of CryoFem Inc.; he succeeds former CEO J. Don Payne, who departed

Polaris Pharmaceuticals Inc., San Diego, Calif.
Business: Cancer, Metabolic
Departed: Robert Hoffman as CFO

Sinovac Biotech Ltd. (NASDAQ:SVA), Beijing, China
Business: Infectious
Resigned: Jacob Chik Keung Ho as CFO; VP of Business Development Nan Wang will become interim CFO

Tobira Therapeutics Inc., Manalapan, N.J.
Business: Infectious
Hired: Helen Jenkins as SVP of program leadership, formerly COO at Nuon Therapeutics Inc.

ViaCyte Inc., San Diego, Calif.
Business: Endocrine, Gene/Cell therapy
Promoted: Kevin D'Amour to CSO from director of stem cell technology
Resigned: John West as president and CEO, while remaining a director; Allan Robins will become acting CEO, while remaining as chief technology officer and a VP

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blepharospasm, hemifacial spasm and post-stroke spasticity in the hand and wrist and to prevent chronic migraine. Botox is also approved in the U.K. to treat dynamic equinus foot deformity in children ≥2 years with cerebral palsy. GlaxoSmithKline has rights from Allergan to develop and commercialize the product in China and Japan.

Almirall S.A. (Madrid:ALM), Barcelona, Spain
Ironwood Pharmaceuticals Inc. (NASDAQ:IRWD), Cambridge, Mass.
Astellas Pharma Inc. (Tokyo:4503), Tokyo, Japan
Forest Laboratories Inc. (NYSE:FRX), New York, N.Y.
Product: Linaclotide
Business: Gastrointestinal

Forest and Ironwood submitted an NDA to FDA for linaclotide to treat chronic constipation and irritable bowel syndrome with constipation. The partners are co-developing and co-marketing the guanylate cyclase C (GCC; GUCY2C) agonist in the U.S. Astellas has exclusive rights from Ironwood to develop and commercialize linaclotide in Japan, Indonesia, Korea, the Philippines, Taiwan and Thailand. Almirall has rights in Europe and the Commonwealth of Independent States (CIS).

Auxilium Pharmaceuticals Inc. (NASDAQ:AUXL), Malvern, Pa.
BioSpecifics Technologies Corp. (NASDAQ:BSTC), Lynbrook, N.Y.
Asahi Kasei Pharma Corp., Tokyo, Japan
Product: Xiapex (Xiaflex - U.S.) collagenase clostridium histolyticum
Business: Musculoskeletal

Auxilium disclosed in its 2Q11 earnings that Swissmedic approved Xiapex collagenase clostridium histolyticum to treat Dupuytren's contracture in adult patients with a palpable cord. Pfizer Inc. (NYSE:PFE, New York, N.Y.), which launched Xiapex in the EU in April, has European marketing rights to the injectable form of collagenase from Auxilium, which has worldwide rights from BioSpecifics. Auxilium markets the product as Xiaflex in the U.S. for the condition, which affects joints in the hand. In March, Auxilium granted Asahi Kasei exclusive rights in Japan *(see BioCentury, March 28)*.

Chugai Pharmaceutical Co. Ltd. (Tokyo:4519), Tokyo, Japan
Roche (SIX:ROG; OTCQX:RHHBY), Basel, Switzerland
Product: RoActemra (Actemra - U.S.) tocilizumab (RG1569)
Business: Autoimmune

The U.K.'s NICE said it needs additional information before it can recommend the use of Roche's RoActemra tocilizumab to treat systemic juvenile idiopathic arthritis in patients who have responded inadequately to NSAIDs, systemic corticosteroids and methotrexate. The agency asked for data comparing RoActemra to other drugs used to treat the disease, data about long-term joint damage and a revised economic model. NICE did say it will not recommend RoActemra for patients who have yet to receive methotrexate, but have received NSAIDs and systemic corticosteroids. Comments are due by Sept. 1, with a second appraisal meeting scheduled for Sept. 14.

Earlier this month, the European Commission approved RoActemra for the indication *(see BioCentury, Aug. 8)*. The product is approved for rheumatoid arthritis in Australia, Brazil, India, Japan and Switzerland, as well as the EU, where it is called RoActemra. In April, FDA approved an expanded label for tocilizumab to include the treatment of systemic juvenile idiopathic arthritis *(see BioCentury, April 25)*. The humanized mAb against IL-6 is approved in the U.S. as Actemra to treat moderate to severe RA and for the inhibition and slowing of joint damage, improvement of physical function and achievement of major clinical response in RA patients. Chugai Pharmaceutical, which is majority-owned by Roche, co-developed the product and markets it in Japan.

Product: Xeloda capecitabine (R340, RG340)
Business: Cancer

The Scottish Medicines Consortium recommended the use of Xeloda capecitabine from Roche on the National Health Service (NHS) in Scotland for the adjuvant treatment of stage III colon cancer following surgery in combination with oxaliplatin. The oral prodrug form of 5-fluorouracil (5-FU) is approved in the EU for the adjuvant treatment of stage III colon cancer following surgery, first-line treatment of advanced gastric cancer in combination with a platinum-based regimen and to treat locally advanced or metastatic breast cancer after failure of cytotoxic chemotherapy and metastatic colorectal cancer. The consortium already recommended the use of Xeloda as monotherapy for adjuvant treatment of stage III colon cancer. Chugai, which is majority owned by Roche, markets Xeloda in Japan.

CombiMatrix Corp. (NASDAQ:CBMX), Mukilteo, Wash.
Product: DNAarray
Business: Diagnostic

CombiMatrix received a clinical laboratory permit from the New York State Department of Health to perform postnatal developmental genetic analysis of patient samples with its DNAarray test. DNAarray uses array comparative genomic hybridization (aCGH) technology for genome-wide evaluation of patient chromosomes to detect developmental disorders, including autism, mental retardation and birth defects.

Cumberland Pharmaceuticals Inc. (NASDAQ:CPIX), Nashville, Tenn.
Product: Caldolor ibuprofen
Business: Neurology

Cumberland disclosed in its 2Q11 earnings that marketing partner Alveda Pharmaceuticals Inc. (Toronto, Ontario) submitted a NDS to Health Canada for Caldolor ibuprofen to treat pain and fever. Alveda has exclusive rights from Cumberland to commercialize Caldolor in Canada *(see BioCentury, May 10, 2010)*. Cumberland markets the IV formulation of ibuprofen in the U.S. to treat pain and fever. The product is also under review in Australia.

Cytori Therapeutics Inc. (NASDAQ:CYTX; Xetra:XMPA), San Diego, Calif.
Product: Adipose-derived regenerative cells (ADRCs)
Business: Cardiovascular

Cytori disclosed in its 2Q11 earnings that it submitted a regulatory application in Europe for ADRCs separated and concentrated using Cytori's Celution 800 System to treat chronic myocardial ischemia. The company expects a response by year end or early next year.

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BioCentury Week in Review (formerly BioCentury Part II)
BioCentury Week in Review is published by
BIOCENTURY PUBLICATIONS INC.,
PO Box 1246 San Carlos CA 94070-1246. Phone 650-595-5333.
Fax 650-595-5589. David Flores, President & CEO;
Karen Bernstein, Ph.D., Chairman & Editor-in-Chief

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DiagnoCure Inc. (TSX:CUR), Québec City, Quebec
Gen-Probe Inc. (NASDAQ:GPRO), San Diego, Calif.
Product: Progensa PCA3 assay
Business: Diagnostic

FDA's Immunology Devices Panel will meet on Oct. 14 to discuss a PMA from Gen-Probe for the Progensa PCA3 assay to aid in determining the need for a repeat biopsy in men suspected of having prostate cancer. The panel is part of the Medical Devices Advisory Committee.

Gen-Probe has exclusive diagnostic rights to the prostate cancer antigen gene 3 (PCA3) gene from DiagnoCure. Gen-Probe markets the assay in the EU, where it has CE mark approval *(see BioCentury, Sept. 27, 2010)*.

Eisai Co. Ltd. (Tokyo:4523; Osaka:4523), Tokyo, Japan
Product: Oral warfarin
Business: Cardiovascular

Eisai disclosed in its fiscal 1Q11 earnings ending June 30 that in July it received Japanese approval for its granule formulation of oral anticoagulant warfarin. Details were not disclosed.

Product: Vasolan verapamil hydrochloride
Business: Cardiovascular

In May, Eisai received Japanese approval to extend the indications of IV and tablet formulations of Vasolan verapamil hydrochloride to include treatment of supraventricular tachyarrhythmia in pediatric patients. The tablet formulation of the calcium channel blocker is approved in Japan to treat tachyarrhythmia, angina, myocardial infarction and other types of ischemic heart disease in adults, while the IV injection formulation is approved to treat tachyarrhythmia in adults.

Eisai Co. Ltd. (Tokyo:4523; Osaka:4523), Tokyo, Japan
Novartis AG (NYSE:NVS; SIX:NOVN), Basel, Switzerland
Product: Banzel rufinamide (Inovelon) (SYN-111)
Business: Neurology

In June, Health Canada approved Banzel rufinamide from Eisai for adjunctive treatment of seizures associated with Lennox-Gastaut Syndrome (LGS) in children ≥4 years of age and adults. Eisai markets the triazole derivative for the indication in Europe as Inovelon and in the U.S. as Banzel. Eisai has exclusive, worldwide rights from Novartis to Banzel for indications other than bipolar mood disorder, anxiety disorders and ophthalmologic disorders. Biotie Therapies Corp. (HSE:BTH1V, Turku, Finland) gained exclusive, worldwide rights to rufinamide to treat anxiety and bipolar mood disorders, except in Japan, through its February acquisition of Synosia Therapeutics AG, which received rights from Novartis *(see BioCentury, April 30, 2007)*.

Endo Pharmaceuticals Holdings Inc. (NASDAQ:ENDP), Chadds Ford, Pa.
Vernalis plc (LSE:VER), Winnersh, U.K.
Product: Frova (Migard - EU) frovatriptan (EN3266)
Business: Neurology

Vernalis disclosed in its 1H11 earnings that Russia approved frovatriptan to treat migraine. Menarini Group (Florence, Italy) has rights to market the selective serotonin (5-HT1B/1D) receptor agonist in Europe, Central America and Brazil. Endo markets frovatriptan as Frova in North America, while SK Chemicals Co. Ltd. (Seoul, South Korea) markets frovatriptan in South Korea.

Genentech Inc., South San Francisco, Calif.
Boehringer Ingelheim GmbH, Ingelheim, Germany
Roche (SIX:ROG; OTCQX:RHHBY), Basel, Switzerland
Product: Actilyse Cathflo alteplase
Business: Other

The Scottish Medicines Consortium (SMC) recommended the restricted use of a 2 mg powder and solvent for injection formulation of Actilyse Cathflo alteplase from Boehringer on the National Health Service (NHS) in Scotland for the thrombolytic treatment of occluded central venous access devices (CVAD) — its approved indication — only when alteplase is the product of choice.

Boehringer markets the tissue plasminogen activator (tPA) outside the U.S., Canada and Japan as Actilyse to treat acute myocardial infarction (MI), acute massive pulmonary embolism (PE) and acute ischemic stroke. Roche's Genentech unit markets the drug as Activase and Cathflo Activase in the U.S., while the Roche Canada unit of Roche markets it in Canada as Cathflo.

Genentech Inc., South San Francisco, Calif.
Teva Pharmaceutical Industries Ltd. (NASDAQ:TEVA), Petah Tikva, Israel
Eli Lilly and Co. (NYSE:LLY), Indianapolis, Ind.
Merck KGaA (Xetra:MRK), Darmstadt, Germany
Novartis AG (NYSE:NVS; SIX:NOVN), Basel, Switzerland
Novo Nordisk A/S (CSE:NVO; NYSE:NVO), Bagsvaerd, Denmark
Pfizer Inc. (NYSE:PFE), New York, N.Y.
Roche (SIX:ROG; OTCQX:RHHBY), Basel, Switzerland
Product: Genotropin somatropin; Humatrope somatropin; Norditropin somatropin; Nutropin somatropin; Nutropin AQ somatropin; Omnitrope somatropin; Saizen somatropin; Tev-Tropin Tjet Injector
Business: Endocrine

FDA updated the ongoing safety review of products containing somatropin recombinant human growth hormone (rhGH) stating that evidence regarding rhGH and an increased risk of death was inconclusive. The agency said a long-term epidemiological study, which had suggested an increased risk of mortality, had design flaws that limited the interpretability of the data. Additionally, medical literature and reports from FDA's adverse event reporting system (AERS) also did not provide evidence of a link. FDA expects additional data from the epidemiological study in the spring 2012. The study evaluated patients treated during childhood for growth hormone deficiency or short stature of unknown cause *(see BioCentury, Jan. 10)*. Somatropin products include: Genotropin from Pfizer; Humatrope from Eli Lilly; Norditropin from Novo Nordisk; Nutropin and Nutropin AQ from Roche's Genentech Inc. unit; Omnitrope from Novartis; Saizen by Merck; and Tev-Tropin Tjet Injector from Teva.

Gilead Sciences Inc. (NASDAQ:GILD), Foster City, Calif.
Johnson & Johnson (NYSE:JNJ), New Brunswick, N.J.
Product: Complera emtricitabine/tenofovir/rilpivirine
Business: Infectious

FDA approved an NDA from Gilead for Complera emtricitabine/tenofovir/rilpivirine to treat HIV-1 infection in treatment-naive patients. Gilead expects to launch Complera in the U.S. this week. The wholesale acquisition cost is $1,704.64 for a 30-day supply. The product is a fixed-dose combination of Johnson & Johnson's Edurant rilpivirine and Gilead's Truvada emtricitabine/tenofovir. Edurant, which FDA approved in May, is a diarylpyrimidine non-nucleoside reverse transcriptase inhibitor (NNRTI), and Truvada is a fixed-dose combination of the nucleoside analog reverse transcriptase inhibitors (NRTI) emtricitabine and tenofovir. J&J's Tibotec Pharmaceuticals Ltd. subsidiary partnered with Gilead in 2009 to develop Complera *(see BioCentury, July 20, 2009)*. Last September, Gilead submitted an MAA to EMA for the combination.

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InterMune Inc. (NASDAQ:ITMN), Brisbane, Calif.
Marnac Inc., Dallas, Texas
Shionogi & Co. Ltd. (Tokyo:4507; Osaka:4507), Osaka, Japan
Product: Esbriet pirfenidone (Pirespa) (S-7701)
Business: Pulmonary

InterMune disclosed in its 2Q11 earnings that in April it launched a named-patient program in major countries of Europe to provide access to Esbriet pirfenidone to treat idiopathic pulmonary fibrosis (IPF) free of charge. The program is expected to last about 12 months. The European Commission approved an MAA for Esbriet for the indication in March. InterMune expects to launch the product in Germany next month, with launches in France, Spain and Italy slated for 1H12. The company also plans to launch Esbriet in the U.K. in 3Q12 and all remaining high priority EU countries during 2012.

InterMune has rights to pirfenidone from Marnac in the U.S., Europe and other territories, while Shionogi has rights in South Korea and Taiwan and markets it as Pirespa for IPF in Japan. Last year, FDA issued a complete response letter for the product for IPF asking for an additional clinical trial despite an agency advisory committee's 9-3 vote recommending approval *(see BioCentury, May 10, 2010)*. Esbriet is a small molecule inhibitor of proinflammatory cytokines such as tumor necrosis factor (TNF) alpha and IL-1 beta, as well as pro-fibrotic cytokines, including platelet derived growth factor (PDGF) and transforming growth factor (TGF) beta.

Kamada Ltd. (Tel Aviv:KMDA), Ness Ziona, Israel
Product: Glassia intravenous Alpha-1 antitrypsin (AAT)
Business: Endocrine

FDA granted Orphan Drug designation for Kamada's IV formulation of alpha-1 antitrypsin (AAT) to treat Type I diabetes. The IV formulation of human plasma derived AAT is in Phase I/II testing for the indication. Baxter International Inc. (NYSE:BAX, Deerfield, Ill.) has exclusive rights to commercialize the IV formulation of AAT in the U.S., Australia, New Zealand and Canada *(see BioCentury, Aug. 30, 2010)*. Baxter markets the compound as Glassia in the U.S. to treat AAT deficiency.

Neoprobe Corp. (NYSE:NEOP), Dublin, Ohio
Product: Lymphoseek tilmanocept
Business: Diagnostic

Neoprobe submitted an NDA to FDA for Lymphoseek tilmanocept for use in intraoperative lymphatic mapping. Lymphoseek is a Tc99m-labeled radioactive tracing agent. In June, Neoprobe filed a formal response to a June 2 Citizen's Petition submitted by hedge fund MSMB Capital Management asking FDA to deny a review and approval of an NDA for Lymphoseek. Neoprobe said the petition is "baseless and replete with factual and regulatory misstatements." The biotech noted MSMB holds a short interest in Neoprobe *(see BioCentury, June 20)*.

New York Blood Center, New York, N.Y.
Product: Hematopoietic progenitor cells from cord blood
Business: Gene/Cell therapy

FDA's Cellular, Tissue and Gene Therapies Advisory Committee will meet on Sept. 22 to discuss a BLA from the not-for-profit New York Blood Center for hematopoietic progenitor cells from cord blood to treat hematologic malignancies, bone marrow failure, primary immunodeficiency diseases, beta thalassemia, Hurler syndrome, Krabbe disease and X-linked adrenoleukodystrophy. The center said FDA directed all public core blood banks to become licensed or qualify for an IND exemption by October 2011 in order to continue providing cord blood units for use in the U.S.

Qiagen N.V. (Xetra:QIA; NASDAQ:QGEN), Venlo, the Netherlands
Product: therascreen K-RAS
Business: Diagnostic

Qiagen submitted a PMA to FDA for its therascreen K-RAS test for use as a companion diagnostic for Erbitux cetuximab to treat metastatic colorectal cancer (mCRC). Qiagen expects a decision on the application next year. The PCR-based test detects mutations in codons 12 and 13 of the K-Ras gene to predict patient response to Erbitux. Erbitux, a chimeric IgG1 mAb targeting EGFR, is approved to treat mCRC and squamous cell carcinoma of the head and neck (SCCHN) in the U.S. and EU. ImClone Systems Inc., a subsidiary of Eli Lilly and Co. (NYSE:LLY, Indianapolis, Ind.), and Bristol-Myers Squibb Co. (NYSE:BMY, New York, N.Y.) market Erbitux in North America. Merck KgaA (Xetra:MRK, Darmstadt, Germany) markets the drug elsewhere, except in Japan where the 3 companies market the drug.

Quidel Corp. (NASDAQ:QDEL), San Diego, Calif.
Product: Quidel Molecular Influenza A+B Real-Time RT-PCR Assay
Business: Diagnostic

Quidel said it received CE Mark for its Quidel Molecular Influenza A+B Real-Time RT-PCR Assay for influenza. Quidel plans to immediately launch the product, which is the company's first molecular diagnostic test, in Europe.

Salix Pharmaceuticals Ltd. (NASDAQ:SLXP), Morrisville, N.C.
Product: Xifaxan rifaximin
Business: Gastrointestinal

Salix disclosed in its 2Q11 earnings that an FDA advisory committee will meet in November to discuss an sNDA for Xifaxan rifaximin 550 mg tablets to treat irritable bowel syndrome (IBS). Salix said the committee will review data for Xifaxan in the indication and provide input on the design of a clinical trial for the retreatment of patients. In March, FDA asked for retreatment information in a complete response letter for the non-absorbed broad-spectrum antibiotic. The company plans to begin a retreatment trial by year end or early 2012. The sNDA is under review to treat non-constipation IBS and IBS-related bloating *(see BioCentury, March 14)*.

The product is already marketed in the U.S. to reduce the risk of overt hepatic encephalopathy (HE) recurrence in patients with advanced liver disease. Salix also markets a 200 mg formulation of Xifaxan in the U.S. to treat travelers' diarrhea.

Teva Pharmaceutical Industries Ltd. (NASDAQ:TEVA), Petah Tikva, Israel
Product: Beclomethasone dipropionate nasal aerosol
Business: Inflammation

FDA accepted for review an NDA from Teva for beclomethasone dipropionate nasal aerosol to treat seasonal and perennial allergic rhinitis. The PDUFA date is March 24, 2012. The product is a nasal aerosol non-aqueous formulation of beclomethasone dipropionate in a hydrofluoroalkane (HFA) metered-dose spray. Teva markets an orally inhaled formulation of beclomethasone dipropionate as Qvar for the maintenance treatment of asthma as prophylactic therapy in patients ages ≥5 years and to treat asthma patients who require systemic corticosteroid administration.

XenoPort Inc. (NASDAQ:XNPT), Santa Clara, Calif.
Astellas Pharma Inc. (Tokyo:4503), Tokyo, Japan
GlaxoSmithKline plc (LSE:GSK; NYSE:GSK), London, U.K.
Product: Horizant gabapentin enacarbil (XP13512, GSK1838262)
Business: Neurology

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GlaxoSmithKline submitted an sNDA to FDA for Horizant gabapentin enacarbil extended-release tablets to manage postherpetic neuralgia (PHN). GSK markets the transported prodrug of gabapentin in the U.S. to treat moderate to severe primary restless legs syndrome. In November, XenoPort reacquired rights outside the U.S. to Horizant after amending a 2007 deal that gave GSK exclusive, worldwide rights outside certain Asian countries *(see BioCentury, Nov. 15, 2010)*. Astellas has exclusive rights to the product in Japan and 5 other Asian countries under a 2005 deal *(see BioCentury, Dec. 5, 2005)*.

CLINICAL RESULTS

Adolor Corp. (NASDAQ:ADLR), Exton, Pa.
Eli Lilly and Co. (NYSE:LLY), Indianapolis, Ind.
Product: ADL5945 (formerly OpRA III)
Business: Gastrointestinal
Molecular target: Mu opioid receptor (OPRM1) (MOR)
Description: Mu opioid receptor (OPRM1; MOR) antagonist
Indication: Treat opioid-induced constipation (OIC)
Endpoint: Change from baseline in weekly average spontaneous bowel movements (SBMs) at week 4; responder rate
Status: Phase II data
Milestone: NA

Top-line data from the double-blind, U.S. Phase II Study 243 trial in 81 chronic non-cancer pain patients with OIC showed that once-daily 0.25 mg ADL5945 met the primary endpoint of significantly increasing the weekly average number of SBMs from baseline to week 4 vs. placebo (2.6 vs. 1.4 SBMs per week, p=0.01). Additionally, ADL5945 non-significantly increased responder rate defined as the proportion of patients achieving ≥3 SBMs per week and an increase of ≥1 SBM per week from baseline vs. placebo (42.5% vs. 29.3%). ADL5945 was well tolerated. Adolor said it plans to initiate pivotal studies as soon as possible. The company has exclusive, worldwide rights to develop and commercialize ADL5945 from Eli Lilly under a 2009 deal *(see BioCentury, Sept. 28, 2009)*.

Indication: Treat opioid-induced constipation (OIC)
Endpoint: Change from baseline in weekly average spontaneous bowel movements (SBMs) at week 4; responder rate, Patient Global Impression of Change (PGIC), bowel movement comfort and satisfaction scores
Status: Phase II data
Milestone: NA

Top-line data from the double-blind, U.S. Phase II Study 242 trial in 131 chronic non-cancer pain patients with OIC showed that twice-daily 0.25 mg ADL5945 met the primary endpoint of significantly increasing the weekly average number of SBMs from baseline to week 4 vs. placebo (3.4 vs. 1.4 SBMs per week, p=0.0003). The twice-daily 0.1 mg dose of ADL5945 missed the endpoint (2 SBMs per week). On secondary endpoints, high-dose ADL5945 significantly improved responder rate defined as the proportion of patients achieving ≥3 SBMs per week and an increase of ≥1 SBM per week from baseline vs. placebo (55.6% vs. 25.6%, p=0.005), but low-dose ADL5945 did not (27.9%). Adolor also said high-dose ADL5945 led to greater improvements from baseline compared to placebo on the exploratory endpoints of PGIC, bowel movement comfort and satisfaction scores. ADL5945 was well tolerated. Adolor said it plans to initiate pivotal studies as soon as possible. The company has exclusive, worldwide rights to develop and commercialize ADL5945 from Eli Lilly under a 2009 deal *(see BioCentury, Sept. 28, 2009)*.

Biogen Idec Inc. (NASDAQ:BIIB), Weston, Mass.
Abbott Laboratories (NYSE:ABT), Abbott Park, Ill.
Product: Daclizumab high-yield process (DAC HYP)
Business: Autoimmune
Molecular target: Interleukin-2 (IL-2) receptor alpha chain (CD25)
Description: Humanized antibody against IL-2 receptor alpha chain (CD25)
Indication: Treat relapsing-remitting multiple sclerosis (RRMS)
Endpoint: Annualized relapse rate (ARR); cumulative number of new gadolinium-enhancing lesions between weeks 8-24, number of new or newly-enlarging T2 hyperintense lesions at 1 year, proportion of patients who relapsed, and quality of life
Status: Phase IIb data
Milestone: NA

Top-line data from the double-blind, international Phase IIb SELECT trial in 600 patients showed that once-monthly 150 and 300 mg subcutaneous daclizumab each met the primary endpoint of ARR compared to placebo. Specifically, low- and high-dose daclizumab reduced ARR by 54% and 50%, respectively, vs. placebo at 1 year (p<0.0001 and p=0.0002, respectively). Compared to placebo, low- and high-dose daclizumab also met the secondary endpoints of significantly reducing the cumulative number of new gadolinium-enhancing lesions between weeks 8-24 (69% and 78%, respectively); the number of new or newly-enlarging T2 hyperintense lesions at 1 year (70% and 79%, respectively); and the proportion of patients who relapsed (55% and 51%, respectively).

Daclizumab missed the secondary endpoint of significantly improving measures of quality of life at 1 year vs. placebo. Furthermore, low- and high-dose daclizumab reduced the risk of sustained disability progression as measured by the expanded disability status scale (EDSS) scores, a tertiary endpoint, by 57% and 43%, respectively, at 1 year vs. placebo. Additionally, the overall incidence of adverse events and treatment discontinuations were similar between treatment groups. There was 1 death in SELECT due to a complication of a psoas muscle abscess in a patient recovering from a serious skin adverse event and 1 death in the ongoing SELECTION extension study due to possible autoimmune hepatitis. The partners said that daclizumab's role in both deaths could not be excluded.

The partners plan to include data from both the SELECT trial and the ongoing Phase III DECIDE trial of daclizumab to treat RRMS in its regulatory applications to FDA and EMA. Biogen Idec did not disclose when it expects data from the DECIDE trial, or when it expects to submit regulatory applications for the product. The DECIDE trial is comparing daclizumab to Biogen Idec's Avonex interferon beta-1a in about 1,500 patients. Abbott gained daclizumab through its 2010 acquisition of Facet Biotech Corp., which partnered with Biogen Idec to develop daclizumab to treat MS in 2005 *(see BioCentury, March 15, 2009)*.

Eli Lilly and Co. (NYSE:LLY), Indianapolis, Ind.
Product: Gemzar gemcitabine
Business: Cancer
Molecular target: Ribonucleotide reductase; DNA polymerase
Description: Nucleoside analog
Indication: Treat advanced non-small cell lung cancer (NSCLC) in elderly patients
Endpoint: Overall survival (OS); 1-year survival
Status: Phase III data
Milestone: NA

Researchers at the Intergroupe Francophone de Cancerologie Thoracique and colleagues reported data from the open-label, French Phase III IFCT-0501 trial in 451 patients ages 70-89 with locally advanced or metastatic NSCLC showing that platinum-based doublet chemo-

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therapy with carboplatin and paclitaxel led to significantly improved median OS vs. monotherapy with either vinorelbine or gemcitabine (10.3 vs. 6.2 months, p<0.0001). Additionally, 44.5% of patients who received the combination therapy were alive at 1 year vs. 25.4% of patients who received either monotherapy. Based on the results, the researchers said that the currently recommended monotherapy regimen for NSCLC patients older than 70 years should be reconsidered. Data were published in *The Lancet*. Eli Lilly markets Gemzar gemcitabine.

Genentech Inc., South San Francisco, Calif.
Chugai Pharmaceutical Co. Ltd. (Tokyo:4519), Tokyo, Japan
Roche (SIX:ROG; OTCQX:RHHBY), Basel, Switzerland
Product: Herceptin trastuzumab (RG597)
Business: Cancer
Molecular target: Epidermal growth factor receptor 2 (EGFR2) (HER2) (ErbB2) (neu)
Description: Humanized mAb against epidermal growth factor receptor 2 (EGFR2; HER2; ErbB2; neu)
Indication: Treat HER2-overexpressing breast cancer in patients >70 years of age
Endpoint: NA
Status: Postmarketing study data
Milestone: NA

Researchers at Vall d'Hebron University Hospital reported data from an analysis of medical records from 45 patients ages 70-92 with HER2-overexpressing breast cancer who had received ≥1 dose of Herceptin showing that the drug increased the incidence of heart problems, especially in women with a history of heart disease and/or diabetes. Specifically, 8 patients experienced asymptomatic cardiotoxicity, defined as an absolute drop of ≥10% in left ventricular ejection fraction (LVEF) with a final LVEF of <50% or any absolute drop of >20%, and 4 patients developed symptomatic congestive heart failure (CHF). All 8 patients with asymptomatic cardiac events recovered completely after discontinuing Herceptin. Furthermore, patients were significantly more likely to develop asymptomatic or symptomatic cardiac events during treatment with Herceptin if they presented with a history of diabetes (33.3% vs. 6.1%, p=0.01) or cardiac disease (33% vs. 9.1%, p=0.017) compared to patients without each respective risk factor. Data were published in *Annals of Oncology*.

The label for Herceptin already includes a boxed warning that the drug can result in subclinical and clinical cardiac failure manifesting as CHF and decreased LVEF, with the greatest risk when administered concurrently with anthracyclines. Herceptin is marketed in the U.S. by Roche's Genentech Inc. unit and by Roche elsewhere. Chugai, which is majority owned by Roche, markets Herceptin in Japan.

Genentech Inc., South San Francisco, Calif.
Roche (SIX:ROG; OTCQX:RHHBY), Basel, Switzerland
Product: Pulmozyme dornase alfa
Business: Infectious
Molecular target: DNA
Description: Recombinant deoxyribonuclease (DNase) for inhalation
Indication: Treat pleural infection
Endpoint: Change from baseline in pleural opacity at day 7; referral for surgery, duration of hospital stay, and safety
Status: NA data
Milestone: NA

The double-blind, U.K. MIST2 trial in 210 patients with pleural infection showed that intrapeural Pulmozyme plus tissue plasminogen activator (tPA) for 3 days significantly reduced mean pleural opacity, the primary endpoint, as measured by the percentage of the ipsilateral hemithorax occupied by effusion on chest radiography from baseline to day 7 vs. placebo (29.5% vs. 17.2%, p=0.005). Pulmozyme and tPA alone led to no significant reductions from baseline in mean pleural opacity vs. placebo (14.7% and 17.2%, respectively, p=0.14 and p=0.55). On secondary endpoints, Pulmozyme plus tPA significantly reduced the frequency of surgical referrals at 3 months (4% vs. 16%, p=0.03) and the duration of hospital stay vs. placebo (11.8 vs. 17 days, p=0.006). Data were published in the *New England Journal of Medicine*. Roche's Genentech Inc. unit markets Pulmozyme in about 70 countries, including the U.S. and Europe, for the improvement of pulmonary function in patients with cystic fibrosis (CF).

Lexicon Pharmaceuticals Inc. (NASDAQ:LXRX), The Woodlands, Texas
Product: Telotristat etiprate (LX1032)
Business: Gastrointestinal
Molecular target: NA
Description: Tryptophan hydroxylase inhibitor
Indication: Treat refractory carcinoid syndrome
Endpoint: Safety; change in bowel movement frequency, relief of symptoms and reduction in serotonin synthesis
Status: Phase II data
Milestone: Start Phase III (mid-2012)

Top-line data from a double-blind, placebo-controlled, U.S. Phase II trial in 23 patients with refractory carcinoid syndrome showed that 5 patients treated with once-daily LX1032 for 28 days achieved a clinical response defined as a reduction of ≥30% in the number of bowel movements per day for ≥2 weeks. Additionally, 6 patients receiving LX1032 reported adequate relief of carcinoid symptoms and 9 patients had a complete biochemical response defined as a reduction of ≥50% in urinary 5-hydroxyindoleacetic acid (5-HIAA), a biomarker of serotonin production. No patients receiving placebo experienced a clinical response, adequate symptom relief or a biochemical response. Lexicon said the trial was not powered to detect statistical significance. Furthermore, the difference between LX1032 and placebo in bowel movement frequency ranged from 1.6-2.9 bowel movements per day across all 4 doses of LX1032, all favoring LX1032. LX1032 was well tolerated. The compound has Fast Track designation in the U.S. to treat carcinoid syndrome and Orphan Drug designation in the EU to treat carcinoid tumors.

Indication: Treat refractory carcinoid syndrome
Endpoint: Safety; number of bowel movements, urinary 5-hydroxyindoleacetic acid (5-HIAA) levels and global assessment of relief of symptoms
Status: Preliminary Phase II data
Milestone: Start Phase III (mid-2012)

Preliminary data from a 12-week, open-label, dose-escalation, European Phase II trial showed that 5 of 6 evaluable patients with refractory carcinoid syndrome treated with thrice-daily LX1032 achieved sustained reductions of ≥30% in bowel movement frequency. Specifically, 2 responses were achieved within the first 4 weeks of therapy, while the remaining 3 responses occurred between 4 and 8 weeks of treatment. LX1032 was well tolerated. Patients received each of thrice-daily 150, 250, 350 and 500 mg LX1032 for 14 days, followed by a 4-week extension period at the optimal dose of the compound. The trial plans to enroll 16 patients. LX1032 has Fast Track designation in the U.S. to treat carcinoid syndrome and Orphan Drug designation in the EU to treat carcinoid tumors.

Oxford BioMedica plc (LSE:OXB), Oxford, U.K.
Product: ProSavin
Business: Neurology

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Molecular target: Not applicable
Description: LentiVector carrying 3 genes encoding enzymes for dopamine synthesis
Indication: Treat Parkinson's disease (PD)
Endpoint: Safety and Unified Parkinson's Disease Rating Score (UPDRS) Part III (motor score) at 6 months; quality of life measures
Status: Additional Phase I/II data
Milestone: Final Phase I/II data (4Q11); submit regulatory application (year end 2011)

Interim data from 3 of 6 evaluable patients in the fourth cohort of an ongoing, open-label, French and U.K. Phase I/II trial showed that quintuple the lowest dose of ProSavin delivered with an enhanced administration method improved motor function on the UPDRS scale from baseline by a mean of 29% at 3 months, with 1 patient showing a 49% improvement. There were no serious adverse events related to ProSavin or the enhanced administration procedure, which delivers higher doses with fewer needles. Oxford BioMedica plans to submit regulatory applications in the U.S. and EU for ProSavin to treat PD by year end.

The company previously reported 3-, 6-, 12-, and 24-month data for the lowest dose of ProSavin; 3-, 6-, and 12-month data for the second dose level delivered without the enhanced procedure; and 3- and 6-month data for the second dose level delivered with the enhanced procedure *(see BioCentury, Sept. 15, 2008; Nov. 24, 2008; July 20, 2009; Oct. 19, 2009; July 12, 2010; & May 9)*.

Repros Therapeutics Inc. (NASDAQ:RPRX), The Woodlands, Texas
Product: Androxal enclomiphene
Business: Endocrine
Molecular target: Not available
Description: Isomer of clomiphene citrate
Indication: Improve glycemic control in men with Type II diabetes and secondary hypogonadism
Endpoint: Change from baseline in HbA1c at 3 months; fasting plasma glucose (FPG)
Status: Interim Phase II data
Milestone: Additional Phase II data (year end 2011)

Interim data from 61 evaluable men with secondary hypogonadism and Type II diabetes in a double-blind, U.S. Phase II trial showed that once-daily 12.5 and 25 mg Androxal significantly increased mean morning testosterone levels from baseline to 3 months vs. placebo. Specifically, low- and high-dose Androxal increased mean morning testosterone levels from 238.2 and 233.8 ng/dL at baseline, respectively, to 463.5 and 444.7 ng/dL at 3 months, whereas placebo increased mean morning testosterone levels from 224.9 ng/dL at baseline to 234.2 ng/dL at 3 months ($p<0.0001$ for both). There was no significant difference between low- and high-dose Androxal. This month, Repros plans to complete enrollment of up to 120 patients ages 20-80 with secondary hypogonadism or adult-onset idiopathic hypogonadotropic hypogonadism (AIHH) who have been diagnosed with Type II diabetes for ≥6 months.

University of Pennsylvania, Philadelphia, Pa.
Product: T cell therapy
Business: Cancer
Molecular target: CD19
Description: Autologous T cells genetically modified *ex vivo* to target CD19, a cell-surface antigen found on chronic lymphocytic leukemia (CLL) cells and normal B cells
Indication: Treat chemotherapy-resistant chronic lymphocytic leukemia (CLL)
Endpoint: NA
Status: Phase I data
Milestone: Complete Phase I (2012)

Researchers at the Perelman School of Medicine at the university reported data from an ongoing Phase I trial showing that 2 of 3 patients with chemotherapy-resistant CLL who received autologous T cells genetically modified *ex vivo* to target CD19 achieved a complete response within 1 month and had sustained remission of their disease. The third patient achieved a partial response. Short-term side effects were induced by cytokine release after tumor cell lysis, and included fever, chills and nausea. The T cells were engineered to express a CD19-specific chimeric antigen receptor (CAR) — a hybrid protein containing an antibody's antigen recognition domain fused to T cell activating domains. The researchers said the modified cells expanded *in vivo* and remained in the patients' blood and bone marrow after treatment. The researchers plan to enroll a total of 10 patients in the trial. Data were published in the *New England Journal of Medicine* and in *Science Translational Medicine*. A Phase II follow-on trial is planned pending funding. The researchers also plan to study this approach in patients with other types of CD19+ tumors, including acute lymphocytic leukemia (ALL) and non-Hodgkin's lymphoma (NHL).

PRECLINICAL RESULTS

Arena Pharmaceuticals Inc. (NASDAQ:ARNA), San Diego, Calif.
Product: Lorcaserin (APD356)
Business: Endocrine
Indication: Weight management, including weight loss and maintenance of weight loss, in obese patients

Arena and partner Eisai Co. Ltd. (Tokyo:4523; Osaka:4523, Tokyo, Japan) reported data from a re-adjudication of female rat mammary tumor diagnoses for lorcaserin in a 2-year carcinogenicity study showing that the percentage of malignant tumors was lower for all dose groups of the obesity candidate than in the initial report included in Arena's 2009 NDA. The companies hope the data will address FDA's concerns about an increased rate of mammary tumors in female rats exposed to the serotonin (5-HT2C) receptor agonist. FDA raised the issue in a complete response letter last October and asked for a blinded re-adjudication of all mammary and lung tissues by a panel of 5 pathologists to better classify between benign and malignant tumors *(see BioCentury, Nov. 1, 2010)*. The initial review of the tissues was conducted by only 1 pathologist. Arena plans to respond by year end.

According to the blinded re-adjudication, 32.3%, 36.9% and 68% of rats receiving 10, 30 and 100 mg/kg/day lorcaserin, respectively, had malignant tumors vs. 40% for undisclosed control-treated rats. In the initial report, 52.3%, 53.9% and 80% of rats receiving low-, mid- and high-dose lorcaserin, respectively, had malignant tumors vs. 43.1% for controls. Additionally, the incidence of benign mammary tumors was higher for all dose groups of lorcaserin compared to Arena's initial report. Specifically, the re-adjudication showed that 83.1%, 84.6% and 68% of rats receiving 10, 30 and 100 mg/kg/day lorcaserin, respectively, had benign tumors vs. 36.9% for controls. In the initial report, 72.3%, 81.5% and 60% of rats receiving low-, mid- and high-dose lorcaserin, respectively, had benign tumors vs. 30.8% for controls. The re-adjudication was conducted by a group of 5 pathologists contracted by Arena in consultation with FDA. The agency has not conducted its own review of the data, according to the company.

FDA has also requested information related to lorcaserin-emergent mammary adenocarcinoma and brain astrocytoma. Earlier this month, the partners reported data to address the brain astrocytoma signal *(see BioCentury, Aug. 8)*. Arena is conducting a 3-month study to

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address the mammary adenocarcinoma signal, but FDA has suggested a 12-month study if the biotech cannot show convincing results with other studies. Arena also plans to submit an MAA for lorcaserin in Europe in 2012. Eisai has marketing rights to lorcaserin in the U.S. *(see BioCentury, July 5, 2010)*.

CytRx Corp. (NASDAQ:CYTR), Los Angeles, Calif.
Product: INNO-206 (formerly DOXO-EMCH)
Business: Cancer
Indication: Treat ovarian cancer

In a mouse xenograft model of ovarian cancer, 24 mg/kg INNO-206 led to significantly greater reductions in tumor size compared to 8 mg/kg doxorubicin. Additionally, mice treated with 12 mg/kg INNO-206 in combination with 4 mg/kg doxorubicin had similar reductions in tumor size to that of mice receiving 24 mg/kg INNO-026 alone. Furthermore, mice treated with INNO-206 alone and doxorubicin alone had body weight loss of 31% and 21%, respectively, compared to only 12% body weight loss for the combination. Data were published in *Investigational New Drugs*. CytRx plans to start Phase IIb testing of the 6-maleimidocaproyl hydrazone prodrug of doxorubicin to treat soft tissue sarcoma (STS) this half. INNO-206 has Orphan Drug designation in the U.S. to treat pancreatic cancer and STS.

iBio Inc. (NYSE-A:IBIO), Newark, Del.
Product: Malaria vaccine
Business: Infectious
Indication: Vaccinate against malaria

In rabbits, iBio's malaria vaccine induced high titers of parasite transmission-blocking antibodies that resulted in a significant >99% reduction in *Plasmodium falciparum* oocyst count from baseline to day 42 post-immunization ($p<0.001$). The vaccine is based on a portion of the Pfs230 antigen from *P. falciparum* and was developed using iBio's iBioLaunch technology. The study was sponsored by the Bill & Melinda Gates Foundation. Data were published in *Clinical and Vaccine Immunology*.

YM BioSciences Inc. (TSX:YM; NYSE-A:YMI), Mississauga, Ontario
Product: CYT387
Business: Cancer
Indication: Treat multiple myeloma (MM)

In vitro, CYT387 time- and dose-dependently inhibited cellular proliferation and induced apoptosis of human myeloma cell lines. Data were published in *Leukemia*. The Janus kinase-1 (JAK-1) and JAK-2 inhibitor is in Phase I/II testing to treat myelofibrosis, for which it has Orphan Drug designation in the U.S. YM gained the compound through its acquisition of Cytopia Ltd. *(see BioCentury, Feb. 8, 2010)*.

CLINICAL STATUS

A.P. Pharma Inc. (OTCQB:APPA), Redwood City, Calif.
Product: APF530
Business: Gastrointestinal
Molecular target: Serotonin (5-HT3) receptor
Description: Granisetron, a serotonin (5-HT3) receptor antagonist formulated using Biochronomer drug delivery technology
Indication: Prevent acute and delayed chemotherapy-induced nausea and vomiting (CINV)
Endpoint: NA
Status: QT/QTc study started
Milestone: QT/QTc study data (1Q12); resubmit NDA (1H12)

A.P. Pharma disclosed in its 2Q11 earnings that in July the company began a thorough QT study of APF530 in healthy volunteers. Last year, A.P. Pharma received a complete response letter from FDA for an NDA for APF530 for the indication. In the letter, A.P. Pharma said the agency asked the company to conduct bioavailability, metabolism and QT studies in volunteers, as well as a reanalysis of selected existing Phase III data. Data from the planned metabolism study and the QT study are expected in 1Q12 *(see BioCentury, May 2)*.

Amarin Corp. plc (NASDAQ:AMRN), Dublin, Ireland
Product: LAX-101, AMR101 (formerly Miraxion)
Business: Cardiovascular
Molecular target: NA
Description: >96% pure ethyl ester of eicosapentaenoic acid (ethyl-EPA)
Indication: Reduce major cardiovascular events
Endpoint: Reduction of first major cardiovascular event
Status: SPA received
Milestone: Submit NDA (3Q11)

Amarin received an SPA from FDA for the international REDUCE-IT cardiovascular outcomes trial to evaluate AMR101 in combination with a statin vs. a statin alone in about 8,000 patients with elevated triglyceride levels and either coronary heart disease (CHD) or risk factors for CHD. REDUCE-IT is slated to begin this year. Amarin plans to submit an NDA to FDA this quarter for AMR101 to treat hypertriglyceridemia based on data from the Phase III MARINE trial *(see BioCentury, May 23)*. Amarin said once REDUCE-IT is underway that it will have met all of the requirements to request approval of AMR101 to treat the mixed dyslipidemia patient population studied in the Phase III ANCHOR trial *(see BioCentury, April 25)*.

Anadys Pharmaceuticals Inc. (NASDAQ:ANDS), San Diego, Calif.
Product: Setrobuvir (ANA598)
Business: Infectious
Molecular target: HCV non-structural protein 5B
Description: Oral non-nucleoside NS5B polymerase inhibitor
Indication: Treat chronic HCV infection
Endpoint: Sustained virological response (SVR) at 24 weeks; undetectable HCV RNA, SVR at week 12, proportion of treatment-naive patients eligible to stop all treatment at week 28, safety
Status: Completed Phase IIb enrollment
Milestone: Phase IIb data (year end 2011)

Anadys disclosed in its 2Q11 earnings that the company completed enrollment of about 275 treatment-naïve and treatment-experienced patients with HCV genotype 1 in a double-blind, international Phase IIb trial comparing 200 mg oral ANA598 given twice daily plus standard of care (SOC; peginterferon alfa-2a and ribavirin) vs. placebo plus SOC. Treatment-naïve patients achieving undetectable levels of virus at week 8 will stop all treatment at week 28, while patients with detectable levels will receive treatment through week 48. ANA598 has Fast Track designation in the U.S. for the indication. Roche (SIX:ROG; OTCQX:RHHBY, Basel, Switzerland) markets Pegasys peginterferon alfa-2a and Copegus ribavirin.

ArQule Inc. (NASDAQ:ARQL), Woburn, Mass.
Daiichi Sankyo Co. Ltd. (Tokyo:4568; Osaka:4568), Tokyo, Japan
Kyowa Hakko Kirin Co. Ltd. (Tokyo:4151), Tokyo, Japan
Product: Tivantinib (ARQ 197)
Business: Cancer
Molecular target: c-Met receptor tyrosine kinase
Description: Small molecule inhibitor of c-Met receptor tyrosine kinase
Indication: Treat non-small cell lung cancer (NSCLC) of non-squamous

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histology
Endpoint: Overall survival (OS); progression-free survival (PFS), objective response rate (ORR) and safety
Status: Phase III started
Milestone: NA

Kyowa Hakko began the double-blind, Asian Phase III ATTENTION trial to compare twice-daily oral tivantinib plus once-daily oral erlotinib vs. placebo plus erlotinib in about 460 patients with locally advanced or metastatic, non-squamous NSCLC with wild-type EGFR who have received 1-2 prior systemic cancer therapies. ArQule is co-developing tivantinib with Daiichi Sankyo on a worldwide basis outside of certain Asian countries, where ArQule licensed rights to Kyowa in 2007 *(see BioCentury, Nov. 17, 2008)*.

Tarceva erlotinib is marketed by OSI Pharmaceuticals Inc., now part of Astellas Pharma Inc. (Tokyo:4503, Tokyo, Japan) and Genentech Inc., a unit of Roche (SIX:ROG; OTCQX:RHHBY, Basel, Switzerland), in the U.S., and by Roche elsewhere.

AVI BioPharma Inc. (NASDAQ:AVII), Bothell, Wash.
Product: Eteplirsen (AVI-4658)
Business: Musculoskeletal
Molecular target: DNA
Description: Phosphorodiamidate morpholino oligomer (PMO) targeting exon 51
Indication: Treat Duchenne muscular dystrophy (DMD)
Endpoint: Dystrophin-positive muscle fibers; CD3, CD4 and CD8 lymphocyte counts
Status: Phase II started
Milestone: NA

AVI BioPharma began a double-blind, placebo-controlled, U.S. Phase II trial to evaluate weekly 30 and 50 mg/kg IV eteplirsen for 24 weeks in 12 patients. The compound has Orphan Drug designation in the U.S. and EU, and Fast Track designation in the U.S. for DMD.

Calando Pharmaceuticals Inc., Pasadena, Calif.
Product: CALAA-01
Business: Cancer
Molecular target: Ribonucleotide reductase
Description: Short interfering RNA (siRNA) duplex targeting the M2 subunit of ribonucleotide reductase (RRM2) delivered via the RONDEL delivery system
Indication: Treat refractory solid tumors
Endpoint: Safety and maximum tolerated dose (MTD); pharmacokinetics, tumor response and immune response
Status: Completed Phase I enrollment
Milestone: Final Phase I data (early 2012)

Arrowhead Research Corp. (NASDAQ:ARWR, Pasadena, Calif.) disclosed in its fiscal 3Q11 earnings ending June 30 that its Calando subsidiary completed enrollment of an undisclosed number of patients in an open-label, dose-escalation, U.S. Phase I trial evaluating 9, 18, 24 or 30 mg/m^2 IV CALAA-01 on days 1, 3, 8, and 10 of a 21-day cycle followed by a second cycle if the first cycle was safe. Additionally, Arrowhead said it will expand into a Phase Ib trial to evaluate different dosing schedules for the compound. The 2 trials combined will enroll up to 36 patients.

Chelsea Therapeutics International Ltd. (NASDAQ:CHTP), Charlotte, N.C.
Dainippon Sumitomo Pharma Co. Ltd. (Tokyo:4506; Osaka:4506), Osaka, Japan
Product: Northera droxidopa
Business: Musculoskeletal
Molecular target: NA
Description: Orally-available synthetic precursor of norepinephrine
Indication: Treat fibromyalgia syndrome (FMS)
Endpoint: Average reduction in pain as measured by the Short Form McGill Pain Questionnaire; Fibromyalgia Index Questionnaire (FIQ), Patient Global Impression of change (PGI-C), Multidimensional Fatigue Inventory (MFI) and Hamilton Anxiety Depression survey (HAMA)
Status: Completed Phase II enrollment
Milestone: Phase II data (year end 2011)

Chelsea completed enrollment of 120 patients in the double-blind, U.K. Phase II FMS201 trial. The 12-arm study is evaluating 200, 400 or 600 mg of oral droxidopa given 3 times daily; 25 or 50 mg carbidopa given 3 times daily; 200/25 mg, 400/25 mg, 600/25 mg, 200/50 mg, 400/50 mg or 600/50 mg of droxidopa/carbidopa given 3 times daily; or placebo. Last year an independent DMC recommended continuation of enrollment in 7 of 12 arms of the trial *(see BioCentury, July 5, 2010)*. Dainippon Sumitomo granted Chelsea rights to droxidopa outside of Japan, Korea, China and Taiwan *(see BioCentury, June 5, 2006)*.

Eisai Co. Ltd. (Tokyo:4523; Osaka:4523), Tokyo, Japan
Product: Ontak denileukin diftitox
Business: Cancer
Molecular target: Interleukin-2 (IL-2) receptor
Description: Interleukin-2 (IL-2) plus diphtheria toxin fusion protein
Indication: Treat peripheral T cell lymphoma (PTCL)
Endpoint: NA
Status: Phase III started
Milestone: NA

Eisai disclosed in its fiscal 1Q11 earnings ending June 30 that it began a U.S. Phase III trial to evaluate Ontak. The product is marketed in the U.S. to treat cutaneous T cell lymphoma (CTCL) in patients who express CD25.

Product: Lenvatinib (E7080)
Business: Cancer
Molecular target: Vascular endothelial growth factor (VEGF) receptor
Description: VEGF receptor tyrosine kinase inhibitor
Indication: Treat thyroid cancer
Endpoint: NA
Status: Phase III started
Milestone: NA

Eisai disclosed in its fiscal 1Q11 earnings ending June 30 that it began the Japanese portion of an international Phase III trial to evaluate lenvatinib.

Emergent BioSolutions Inc. (NYSE:EBS), Rockville, Md.
Product: Tuberculosis vaccine (MVA85A/AERAS-485) (formerly MVA85A)
Business: Infectious
Molecular target: NA
Description: Recombinant modified vaccinia Ankara (rMVA) expressing antigen 85A
Indication: Prevent tuberculosis (TB)
Endpoint: Immunogenicity and preventing TB disease
Status: Phase IIb started
Milestone: NA

The Oxford-Emergent Tuberculosis Consortium Ltd., a JV between Emergent and University of Oxford (Oxford, U.K.), and not-for-profit Aeras Global TB Vaccine Foundation (Rockville, Md.) began a double-blind, placebo-controlled, African Phase IIb trial to evaluate MVA85A/

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AERAS-485 in about 1,400 HIV-infected patients ages 18-50.

The JV was formed under a 2008 deal to develop the university's vaccine to prevent TB *(see BioCentury, July 28, 2008)*. European and Developing Countries Clinical Trials Partnership (EDCTP) is providing funding for the trial. The vaccine has Orphan Drug designation in the EU for the indication.

Exelixis Inc. (NASDAQ:EXEL), South San Francisco, Calif.
Product: Cabozantinib (XL184)
Business: Cancer
Molecular target: Vascular endothelial growth factor (VEGF) receptor 2 (KDR/Flk-1) (VEGFR-2); c-Met receptor tyrosine kinase
Description: Spectrum-selective kinase inhibitor of vascular endothelial growth factor (VEGF) receptor 2 (KDR/Flk-1) and c-Met receptor tyrosine kinase
Indication: Treat metastatic castration-resistant prostate cancer (CRPC)
Endpoint: Bone scan response and improvement of bone pain
Status: SPA submitted
Milestone: Start Phase III (year end 2011)

Exelixis submitted a protocol to FDA to request an SPA for the planned Phase III XL184-306 trial to evaluate cabozantinib. Exelixis expects to begin the trial by year end.

Glenmark Pharmaceuticals Ltd. (NSE:GLENMARK; BSE:532296), Mumbai, India
Product: Revamilast (GRC 4039)
Business: Autoimmune
Molecular target: Phosphodiesterase-4 (PDE-4)
Description: Phosphodiesterase-4 (PDE-4) inhibitor
Indication: Treat rheumatoid arthritis (RA)
Endpoint: Efficacy; safety
Status: Phase IIb started
Milestone: Phase IIb data (2Q12)

Glenmark began a double-blind, placebo-controlled, international Phase IIb trial to evaluate 3 doses of Revamilast in >400 patients.

Business: Inflammation
Molecular target: Phosphodiesterase-4 (PDE-4)
Description: Phosphodiesterase-4 (PDE-4) inhibitor
Indication: Treat chronic asthma
Endpoint: Lung function as measured by forced expiratory volume in 1 second (FEV1); safety
Status: Phase IIb started
Milestone: Phase IIb data (2Q12)

Glenmark began a 12-week, double-blind, placebo-controlled, international Phase IIb trial to evaluate 3 doses of Revamilast in about 450 patients.

Immune Network Ltd. (Pink:IMMFF), Vancouver, B.C.
Product: V7
Business: Infectious
Molecular target: NA
Description: Oral therapeutic vaccine comprising heat-inactivated Mycobacterium
Indication: Treat pulmonary tuberculosis (TB) infection
Endpoint: Sputum conversion at 2 months; safety
Status: Phase II started
Milestone: NA

Immune Network said its Immunitor Inc. business began the double-blind, Ukrainian Phase II imm02 trial to evaluate once-daily oral V7 plus standard of care (SOC) vs. placebo plus SOC in about 40 TB patients.

Infinity Pharmaceuticals Inc. (NASDAQ:INFI), Cambridge, Mass.
Product: Retaspimycin (IPI-504)
Business: Cancer
Molecular target: Heat shock protein 90 (Hsp90)
Description: Small molecule Hsp90 chaperone inhibitor
Indication: Treat non-small cell lung cancer (NSCLC)
Endpoint: Overall response rate (ORR); progression-free survival (PFS), time to progression and overall survival (OS)
Status: Phase Ib/II started
Milestone: NA

Infinity began a dose-escalation, U.S. Phase Ib/II trial to evaluate 450 mg/m^2 IV retaspimycin weekly in combination with Afinitor everolimus from Novartis AG (NYSE:NVS; SIX:NOVN, Basel, Switzerland) in up to 45 NSCLC patients with K-Ras mutations. Afinitor is approved in the U.S. and EU to treat advanced kidney cancer, as Certican to prevent transplant rejection in over 80 countries, and as Zortress in the U.S. to prevent organ rejection of kidney transplants in adult patients at low to moderate immunologic risk. Afinitor is also approved in the U.S. to treat subependymal giant cell astrocytomas (SEGA) associated with tuberous sclerosis (TS) and is under review in the EU for SEGA associated with TS and neuroendocrine tumors of pancreatic origin.

Infinity Pharmaceuticals Inc. (NASDAQ:INFI), Cambridge, Mass.
Mundipharma International Ltd., Cambridge, U.K.
Product: IPI-926
Business: Cancer
Molecular target: Smoothened (SMO)
Description: Hedgehog pathway inhibitor derived from cyclopamine
Indication: Treat advanced pancreatic cancer
Endpoint: Maximum tolerated dose (MTD); time to tumor progression, objective response rate (ORR) and safety
Status: Phase Ib/II started
Milestone: NA

Infinity said investigators began an open-label, U.S. Phase Ib/II trial to evaluate 130-160 mg/day oral IPI-926 in combination with FOLFIRINOX (5-fluorouracil (5-FU), leucovorin, irinotecan, and oxaliplatin) chemotherapy in about 20 patients. Mundipharma partnered with Infinity to co-develop and commercialize IPI-926 in a 2008 cancer deal. Infinity has rights to commercialize IPI-926 in the U.S., while Mundipharma has rights elsewhere *(see BioCentury, Nov. 24, 2008)*.

Inhibitex Inc. (NASDAQ:INHX), Alpharetta, Ga.
Pfizer Inc. (NYSE:PFE), New York, N.Y.
Product: SA4Ag
Business: Infectious
Molecular target: NA
Description: *Staphylococcus aureus* vaccine composed of 4 antigens
Indication: Prevent *S. aureus* infection
Endpoint: Safety and immunogenicity
Status: Phase I/II started
Milestone: NA

Inhibitex disclosed in its 2Q11 earnings that partner Pfizer began a double-blind Phase I/II trial to evaluate 3 ascending doses of SA4Ag in 1,068 healthy adult volunteers. The trial start triggered a $1 million milestone payment to Inhibitex under a 2001 deal with Wyeth, which Pfizer acquired in 2009. Pfizer has exclusive, worldwide rights to Inhibitex's MSCRAMM protein platform to develop and commercialize vaccines for Staphylococcal infections *(see BioCentury, Sept. 24, 2001 & Oct. 19, 2009)*.

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Innate Pharma S.A. (Euronext:IPH), Marseille, France
Novo Nordisk A/S (CSE:NVO; NYSE:NVO), Bagsvaerd, Denmark
Product: Anti-NKG2a (IPH 2201, NN8765-3658) (formerly IPH22XX)
Business: Autoimmune
Molecular target: Killer cell lectin-like receptor subfamily C member 1 (KLRC1) (CD159a) (NKG2A)
Description: mAb against killer cell lectin-like receptor subfamily C member 1 (KLRC1; CD159a; NKG2A)
Indication: Treat rheumatoid arthritis (RA)
Endpoint: Safety and pharmacokinetics
Status: Phase I started
Milestone: NA

Novo Nordisk disclosed in its 1H11 earnings that in May it began a double-blind, placebo-controlled, dose-escalation, German Phase I trial to evaluate single doses of subcutaneous and IV anti-NKG2a and multiple doses of subcutaneous anti-NKG2a in about 52 patients. Novo Nordisk has rights to anti-NKG2a from Innate under a 2003 deal that granted Novo Nordisk rights to receptor targets expressed by natural killer (NK) cells. The discovery portion of the deal expired in March 2009, but license rights to the compounds developed under the deal are still in effect *(see BioCentury, May 11, 2009)*.

Isis Pharmaceuticals Inc. (NASDAQ:ISIS), Carlsbad, Calif.
OncoGenex Pharmaceuticals Inc. (NASDAQ:OGXI), Bothell, Wash.
Teva Pharmaceutical Industries Ltd. (NASDAQ:TEVA), Petah Tikva, Israel
Product: Custirsen sodium (TV-1011) (OGX-011)
Business: Cancer
Molecular target: Clusterin mRNA
Description: Second-generation antisense inhibitor of serum clusterin mRNA
Indication: Treat advanced non-small cell lung cancer (NSCLC)
Endpoint: Survival benefit
Status: Phase III delayed
Milestone: NA

OncoGenex disclosed in its 2Q11 earnings that it will delay the start of a Phase III trial of OGX-011 in combination with first-line chemotherapy after partner Teva reported data from a drug-drug interaction study showing that OGX-011 may inhibit enzymes that metabolize paclitaxel. OncoGenex had planned to evaluate OGX-011 plus paclitaxel in the trial, which was slated to begin this year. OncoGenex said that it will consider other combinations while Teva completes additional drug interaction studies.

OncoGenex granted Teva exclusive, worldwide rights to develop and commercialize OGX-011 in 2009 *(see BioCentury, Jan. 4, 2010)*. OncoGenex has access to Isis' antisense chemistry for use with custirsen under an amended 2001 deal *(see BioCentury, July 21, 2008)*.

Indication: Treat castration-resistant prostate cancer (CRPC)
Endpoint: Durable pain palliation for ≥12 weeks; time to pain progression and safety
Status: Phase III ongoing
Milestone: Phase III data (4Q13)

OncoGenex reported in its 2Q11 earnings that data on the primary endpoint from the double-blind, placebo-controlled international Phase III SATURN trial of custirsen plus docetaxel/prednisone as second-line chemotherapy will be delayed to 4Q13 from 2Q13 due to slow enrollment. Earlier this year, the company submitted a revised SPA to FDA for the trial to expand the patient population to include docetaxel re-treatment or cabazitaxel as second-line chemotherapy. SATURN plans to enroll about 300 men who have progressed after first-line docetaxel therapy.

However, OncoGenex said the agency indicated that an NDA for OGX-011 for the indication supported primarily by the results of the Phase III SYNERGY trial in about 800 CRPC patients alone would be acceptable for submission. Survival data from SYNERGY are expected 4Q13. SYNERGY is also evaluating docetaxel/prednisone with or without custirsen.

OncoGenex granted Teva exclusive, worldwide rights to develop and commercialize custirsen in 2009 *(see BioCentury, Jan. 4, 2010)*. OncoGenex has access to Isis' antisense chemistry for use with custirsen under an amended 2001 deal *(see BioCentury, July 21, 2008)*. Sanofi (Euronext:SAN; NYSE:SNY, Paris, France) markets Jevtana cabazitaxel.

MannKind Corp. (NASDAQ:MNKD), Valencia, Calif.
Product: Afrezza (formerly Afresa)
Business: Endocrine
Molecular target: Insulin receptor (INSR)
Description: Dry powder formulation of insulin plus an inhaler
Indication: Treat Type I and Type II diabetes
Endpoint: Change in HbA1c from baseline
Status: Phase III start
Milestone: Start Phase III (3Q11); complete Phase III (year end 2012)

MannKind said FDA confirmed the protocols of 2 Phase III trials of Afrezza requested by FDA in a January complete response letter. The open-label, international Phase III Study 171 trial will compare Afrezza using the inhaler MannKind used in Phase III testing vs. Afrezza administered via the MedTone commercial inhaler or injected rapid-acting insulin in Type I diabetics. The placebo-controlled, international Phase III Study 174 trial will evaluate Afrezza using the inhaler MannKind used in Phase III testing in Type II diabetics who are inadequately controlled on metformin with or without a second or third oral medication. The primary endpoint for both trials is the change from baseline in HbA1c level. The trials are expected to begin this quarter and to complete by year end 2012, with an NDA resubmission slated for about 2 months thereafter. Details were not disclosed.

In the January letter, the agency requested 1 trial each in Type I and II diabetes, with at least 1 of the trials including a comparison of patients treated with the MedTone inhaler vs. the inhaler MannKind used in Phase III testing. FDA issued the first complete response letter in March 2010 for the dry powder formulation of insulin plus an inhaler. MannKind previously said it hoped to complete the 2 trials in 2H12 *(see BioCentury, March 22, 2010 & Jan. 24, 2011)*.

Neovacs S.A. (Euronext:ALNEV), Paris, France
Product: TNF-Kinoid (formerly TNFalpha kinoid)
Business: Autoimmune
Molecular target: Tumor necrosis factor (TNF) alpha
Description: Immunotherapy against tumor necrosis factor (TNF) alpha
Indication: Treat rheumatoid arthritis (RA)
Endpoint: Optimal dosing; safety and efficacy as measured by American College of Rheumatology and European League Against Rheumatism (EULAR) criteria and disease activity score using 28 joint counts (DAS28)
Status: Completed Phase IIa enrollment
Milestone: Interim Phase IIa data (2H11); Final Phase IIa data (year end 2011)

Neovacs completed enrollment of 40 patients in the double-blind, placebo-controlled, international Phase IIa TFN-K-003 trial evaluating 90, 180 and 360 µg intramuscular TNF-Kinoid given on days 0, 7 and 28 or days 0 and 28.

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Novavax Inc. (NASDAQ:NVAX), Rockville, Md.
Product: RSV-F vaccine
Business: Infectious
Molecular target: NA
Description: Respiratory syncytial virus (RSV) vaccine directed against the viral fusion F protein and formulated in virus-like particles (VLPs)
Indication: Vaccinate against respiratory syncytial virus (RSV) infection
Endpoint: Safety; immunogenicity
Status: Completed Phase I enrollment
Milestone: Interim Phase I data (3Q11)

Novavax completed enrollment of about 150 healthy volunteers ages 18-49 in a double-blind, placebo-controlled, dose-escalation, U.S. Phase I trial evaluating 2 doses of intramuscular RSV-F vaccine given about 30 days apart. Patients will receive 5, 15 and 30 µg RSV-F with adjuvant or 30 µg RSV-F without adjuvant. Last year, FDA lifted a clinical hold on an IND for the trial after Novavax resolved a question regarding chemistry, manufacturing and controls (CMC) *(see BioCentury, Nov. 15, 2010)*.

Novo Nordisk A/S (CSE:NVO; NYSE:NVO), Bagsvaerd, Denmark
Product: IDegLira
Business: Endocrine
Molecular target: Glucagon-like peptide-1 receptor (GLP-1R) (GLP1R)
Description: Fixed ratio combination of Victoza liraglutide, a long-acting analog of glucagon-like peptide-1 (GLP-1), and insulin degludec, a long-acting insulin analog
Indication: Treat Type II diabetes
Endpoint: Change in HbA1c from baseline to week 26; change in body weight, number of hypoglycemic episodes, daily insulin dose, change from baseline in incremental area under the curve 0-4h (iAUC0-4h) derived from the glucose concentration profile during meal test
Status: Phase IIIa started
Milestone: NA

Novo Nordisk disclosed in its 1H11 earnings that in May it began the first of 2 open-label, international Phase IIIa trials to evaluate IDegLira vs. insulin degludec or liraglutide alone for 26 weeks in 1,660 Type II diabetics. The company plans to submit regulatory applications in the U.S. and EU for insulin degludec to treat diabetes this half. Novo Nordisk markets Victoza liraglutide.

Product: Vatreptacog alfa (rFVIIa) (formerly NN1731)
Business: Hematology
Molecular target: Factor VIIa
Description: Recombinant Factor VIIa analog
Indication: Treat acute bleeding episodes in patients with congenital hemophilia and inhibitors
Endpoint: Effective bleeding control defined as no additional hemostatic medication; effective and sustained bleeding control, number of doses of trial product given for each acute bleed, safety and immunogenicity
Status: Phase IIIa started
Milestone: NA

Novo Nordisk disclosed in its 1H11 earnings that in July it began a double-blind, international Phase IIIa trial to compare vatreptacog alfa vs. NovoSeven in 60 patients. Novo Nordisk markets NovoSeven, a recombinant human coagulation Factor VIIa, for hemophilia and congenital Factor VII deficiency.

Product: Victoza liraglutide (NN2211)
Business: Endocrine
Molecular target: Glucagon-like peptide-1 receptor (GLP-1R) (GLP1R)
Description: Long-acting analog of glucagon-like peptide-1 (GLP-1)
Indication: Treat obesity
Endpoint: Change from baseline in fasting body weight and proportion of patients losing at least ≥5% or >10% baseline body weight; change from baseline in HbA1c, proportion of patients reaching target HbA1c <7% or ≤6.5%, change from baseline in waist circumference and change in fasting body weight
Status: Phase IIIa started
Milestone: NA

Novo Nordisk disclosed in its 1H11 earnings that in June it began a double-blind, placebo-controlled, international Phase IIIa trial to evaluate 1.8 and 3 mg subcutaneous liraglutide once daily for 56 weeks in 800 overweight or obese Type II diabetics. The trial is part of the company's Phase III SCALE program evaluating liraglutide to treat obesity in patients with and without diabetes. Novo Nordisk markets liraglutide as Victoza to treat Type II diabetes.

Indication: Treat obesity
Endpoint: Change from baseline in body weight, proportion of patients losing ≥5% or >10% baseline body weight and the proportion of patients with onset Type II diabetes; change from baseline in waist circumference and pre-diabetes status, mean change from baseline in body weight, proportion of patients losing ≥5% and >10% baseline body weight and change from baseline in fasting body weight
Status: Phase IIIa started
Milestone: NA

Novo Nordisk disclosed in its 1H11 earnings that in June it began a double-blind, placebo-controlled international Phase IIIa trial to evaluate 3 mg subcutaneous liraglutide once daily for 56 weeks in patients that are not pre-diabetic and for 160 weeks in pre-diabetics. The trial, which is slated to enroll about 3,600 non-diabetic obese or overweight patients, is part of the company's Phase III SCALE program evaluating liraglutide to treat obesity in patients with and without diabetes. Novo Nordisk markets liraglutide as Victoza to treat Type II diabetes.

Orexo AB (SSE:ORX), Uppsala, Sweden
Product: OX219 (formerly PKX219)
Business: Neurology
Molecular target: NA
Description: Sublingual tablet formulation of buprenorphine and naloxone
Indication: Treat opioid dependency
Endpoint: Dosing
Status: Phase I started
Milestone: Phase I data (3Q11)

Orexo began a Phase I trial to evaluate OX219 in healthy volunteers. Orexo is developing the compound under section 505(b)(2) of the Food, Drug and Cosmetic Act, which allows sponsors to reference data on safety and efficacy from the scientific literature or from previously approved products.

Pharming Group N.V. (Euronext:PHARM), Leiden, the Netherlands
Product: Rhucin (Ruconest - EU) conestat alfa (rhC1INH)
Business: Cardiovascular
Molecular target: Complement 1 (C1) esterase
Description: Recombinant human complement 1 (C1) esterase inhibitor
Indication: Treat acute attacks of hereditary angioedema (HAE)
Endpoint: Time to beginning of relief based on the visual analog scale (VAS); minimal important difference (MID) of the overall VAS score, time to beginning of relief based on MID and on the investigator score, and safety
Status: SPA received
Milestone: Complete Phase III (3Q12)

Pharming received an SPA from FDA after amending the protocol for an ongoing, double-blind, placebo-controlled Phase III trial evaluating IV

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Rhucin. In May, Pharming amended the trial to increase enrollment to about 75 from 50 patients and to modify the manner in which the primary endpoint is assessed to address issues raised by FDA after the agency refused to file a BLA for Rhucin *(see BioCentury, March 7 & May 9)*. The protocol was also amended to include open-label doses of Rhucin as a rescue medication.

The product is approved as Ruconest in the EU to treat acute attacks of HAE. Swedish Orphan Biovitrum AB (SSE:SOBI, Stockholm, Sweden) has rights to distribute Ruconest in 24 countries in the EU plus Norway, Iceland and Switzerland, while Santarus Inc. (NASDAQ:SNTS, San Diego, Calif.) has exclusive commercialization rights in North America.

Portola Pharmaceuticals Inc., South San Francisco, Calif.
Novartis AG (NYSE:NVS; SIX:NOVN), Basel, Switzerland
Product: Elinogrel (PRT060128, PRT128)
Business: Cardiovascular
Molecular target: Purinergic receptor P2Y G protein-coupled 12 (P2RY12) (P2Y12)
Description: Reversible purinergic receptor P2Y G protein-coupled 12 (P2RY12; P2Y12) antagonist
Indication: Treat chronic coronary heart disease
Endpoint: NA
Status: Suspended Phase III enrollment
Milestone: NA

Novartis suspended the placebo-controlled Phase III ECLIPSE trial to evaluate elinogrel in patients with chronic coronary heart disease to prioritize development of the compound in acute coronary syndrome (ACS). The pharma said the compound may offer significant positive benefits over existing therapies in ACS. Details were not disclosed. Novartis has exclusive, worldwide rights to elinogrel from Portola under a 2009 deal *(see BioCentury, Feb. 16, 2009)*.

Progenics Pharmaceuticals Inc. (NASDAQ:PGNX), Tarrytown, N.Y.
Salix Pharmaceuticals Ltd. (NASDAQ:SLXP), Morrisville, N.C.
Product: Oral Relistor methylnaltrexone (MNTX) (MOA-728)
Business: Gastrointestinal
Molecular target: Mu opioid receptor (OPRM1) (MOR)
Description: Peripheral mu opioid receptor (MOR) antagonist
Indication: Treat opioid-induced constipation (OIC)
Endpoint: Proportion of subjects with rescue-free bowel movement; time and frequency of rescue-free bowel movements
Status: Completed Phase III enrollment
Milestone: Phase III data (year end 2011 - early 2012)

Salix disclosed in its 2Q11 earnings that in July it completed enrollment of about 700 patients with chronic non-cancer pain in a double-blind, placebo-controlled, international Phase III trial to evaluate 3 doses of oral Relistor. Partner Progenics submitted an sNDA to FDA in June for subcutaneous Relistor to treat OIC in patients with chronic, non-cancer pain *(see BioCentury, July 4)*. The subcutaneous formulation is approved in more than 50 countries, including the U.S. and those of the EU, to treat OIC in patients receiving palliative care when response to laxative therapy has not been sufficient. Salix has exclusive, worldwide rights from Progenics to develop and commercialize all formulations of Relistor, excluding Japan, where Ono Pharmaceutical Co. Ltd. (Tokyo:4528; Osaka:4528, Osaka, Japan) has rights to the subcutaneous formulation *(see BioCentury, Feb. 14)*.

Sygnis Pharma AG (Xetra:LIOK), Heidelberg, Germany
Product: AX200
Business: Neurology
Molecular target: Granulocyte colony-stimulating factor (G-CSF) receptor (CD114)
Description: Endogenous granulocyte colony-stimulating factor (G-CSF) protein
Indication: Treat acute ischemic stroke
Endpoint: Efficacy as measured by the modified Rankin Scale (mRS); functional ability on 1 hand, safety and changes in infarct size on the other hand using imaging
Status: Completed Phase II enrollment
Milestone: Preliminary Phase II data (year end 2011)

Sygnis completed enrollment of 328 patients who had an ischemic stroke within 9 hours in the double-blind, placebo-controlled, European Phase II AXIS 2 trial evaluating a 3-day continuous IV infusion of AX200. In March, an independent DSMB recommended continuation of AXIS 2 for the third and final time after reviewing data from 75% of the planned 328 patients *(see BioCentury, March 28)*.

Synta Pharmaceuticals Corp. (NASDAQ:SNTA), Lexington, Mass.
Product: Ganetespib (STA-9090)
Business: Cancer
Molecular target: Heat shock protein 90 (Hsp90)
Description: Small molecule heat shock protein 90 (Hsp90) inhibitor
Indication: Treat metastatic castration-resistant prostate cancer (CRPC)
Endpoint: Reduction in androgen receptor transcriptional activity; progression-free survival (PFS), overall survival (OS), response rate based on RECIST criteria and safety
Status: Phase II started
Milestone: NA

Synta disclosed in its 2Q11 earnings that investigators at the Dana-Farber Cancer Institute began an open-label, U.S. Phase II trial to compare 200 mg/m^2 IV ganetespib given weekly for the first 3 weeks of a 28-day cycle in combination with 3.5 mg oral Avodart dutasteride daily vs. ganetespib alone in about 30 patients. GlaxoSmithKline plc (LSE:GSK; NYSE:GSK, London, U.K.) markets Avodart.

Trius Therapeutics Inc. (NASDAQ:TSRX), San Diego, Calif.
Dong-A Pharmaceutical Co. Ltd. (KSE:000640), Seoul, South Korea
Bayer AG (Xetra:BAY), Leverkusen, Germany
Product: Torezolid phosphate (TR-701) (formerly DA-7218)
Business: Infectious
Molecular target: Ribosomal 50S subunit
Description: Second generation oxazolidinone, a bacterial protein biosynthesis inhibitor
Indication: Treat acute bacterial skin and skin structure infection (ABSSSI)
Endpoint: Non-inferiority to Zyvox in cessation of spread of infected lesions and absence of fever after 48-72 hours after initiation of therapy (superiority will be assessed if non-inferiority endpoint is met); sustained clinical response at the end of therapy visit, investigator's assessment of clinical response at all visits and clinical success at the post-treatment evaluation visit
Status: SPA received
Milestone: Start Phase III (4Q11)

Trius received an SPA from FDA for a double-blind Phase III trial evaluating once-daily 200 mg IV and oral torezolid for 6 days vs. twice-daily 600 mg Zyvox linezolid for 10 days in 658 patients. Patients will receive the IV torezolid for ≥1 day and then oral torezolid at the investigator's discretion. Trius plans to begin the trial next quarter.

Last month, Trius granted Bayer exclusive rights to torezolid in China, Japan, Africa, Latin America, the Middle East, and all other countries in Asia, excluding North and South Korea *(see BioCentury, Aug. 1)*. Trius in-licensed torezolid outside North and South Korea from Dong-A *(see BioCentury, March 5, 2007)*. Pfizer Inc. (NYSE:PFE, New York, N.Y.) markets Zyvox.

OFFERINGS & SECURITIES TRANSACTIONS

Week ended 8/12/11. Shares after offering refers to shares outstanding. Proceeds are gross, not net. Shares offered don't include overallotments. Currency rates used in the week: C$=US$1.0191;€=$1.4357;£=$1.6425

Completed Offerings

Acutus Medical Inc., San Diego, Calif.
Business: Cardiovascular
Date completed: 8/8/11
Type: Venture financing
Raised: $1 million
Investors: Index Ventures; private investors

Agenus Inc. (NASDAQ:AGEN), Lexington, Mass.
Business: Cancer, Infectious
Date completed: 8/11/11
Type: Follow-on
Raised: $7 million
Shares: 13.7 million
Price: $0.51
Shares after offering: 127.8 million
Underwriters: William Blair; Gleacher

Enobia Pharma Inc., Montreal, Quebec
Business: Metabolic
Date completed: 8/8/11
Type: Venture financing
Raised: $40 million
Investors: New investors
Placement agent: BofA Merrill Lynch

IntelGenx Corp. (TSX-V:IGX; OTCBB:IGXT), Ville St-Laurent, Quebec
Business: Drug delivery
Date completed: 8/9/11
Type: Warrant exercise
Raised: $500,000
Shares: 920,652
Shares after offering: 46.2 million
Note: IntelGenx said it issued 920,652 shares through the exercise of warrants and stock options subsequent to the end of 2Q11.

Jennerex Inc., San Francisco, Calif.
Business: Cancer
Date completed: 8/11/11
Type: Venture financing
Raised: $8.6 million
Investors: Existing investors; new investors

Knome Inc., Cambridge, Mass.
Business: Genomics
Date completed: 8/2/11
Type: Venture financing
Raised: $5 million
Investors: Not disclosed
Note: The company raised $5 million in the first close of a planned $20 million series B round.

Microbix Biosystems Inc. (TSX: MBX), Toronto, Ontario
Business: Generics, Infectious, Supply/Service
Date completed: 8/4/11
Type: Private placement of units
Raised: C$359,258 (US$366,120)
Units: 1 million
Price: C$0.35 (unit)
Shares after offering: 57.2 million
Note: Microbix raised C$359,258 (US$366,120) in the second tranche of a unit offering, bringing the total raised to C$569,258 (US$584,919). The company raised C$210,000 (US$218,799) in July. Each unit comprises a share and a two-year warrant to purchase 0.5 shares, with each whole warrant exercisable at C$0.45.

NeurogesX Inc. (NASDAQ: NGSX), San Mateo, Calif.
Business: Neurology
Date completed: 8/8/11
Type: Debt financing
Raised: $15 million
Investor: Hercules Technology Growth Capital
Note: The debt is a 42-month loan, which bears interest at the greater of 9.5% and 9.5% plus the positive difference between the prime rate and 3.25%. NeurogesX also secured a revolving line of credit with the investor for up to $5 million. The line of credit matures Dec. 31, 2012, and bears interest at the greater of 6.75% and 6.75% plus the positive difference between the prime rate and 3.25%. The investor also received a five-year warrant to purchase up to 791,667 shares at $1.80.

PharmaGap Inc. (TSX-V:GAP), Ottawa, Ontario
Business: Cancer, ADMET
Date completed: 8/4/11
Type: Private placement of units
Raised: C$416,800 (US$424,761)
Units: 4.6 million
Price: C$0.09 (unit)
Shares after offering: 128.4 million
Placement agent: Northern Securities
Note: PharmaGap raised C$416,800 (US$424,761) in the final close of a private placement, bringing the total raised to C$496,405 (US$507,256). The company raised C$79,605 (US$82,495) in a first close in July. Each unit comprises a share and a two-year warrant to purchase a share at C$0.14.

Second Genome Inc., San Francisco, Calif.
Business: Supply/Service
Date completed: 8/9/11
Type: Venture financing
Raised: $5 million
Investors: Advanced Technology Ventures; Morgenthaler Ventures; Wavepoint Ventures; Seraph Group; individual investors

Sygnis Pharma AG (Xetra: LIOK), Heidelberg, Germany
Business: Neurology
Date completed: 8/10/11
Type: Private placement
Raised: €6.2 million ($8.8 million)
Shares: 3.1 million
Price: €2
Shares after offering: 16.8 million
Investors: dievini Hopp BioTech; existing investors
Note: Shareholders were eligible to purchase four shares for every 17 held.

T2 Biosystems Inc., Lexington, Mass.
Business: Diagnostic
Date completed: 8/10/11
Type: Venture financing
Raised: $23 million
Investors: Aisling Capital; Flagship Ventures; Polaris Venture Partners; Flybridge Capital Partners; Physic Ventures; Partners Healthcare; Arcus Ventures; RA Capital; Camros Capital; WS Investment

UgiChem GmbH, Innsbruck, Austria
Business: Drug delivery
Date completed: 8/6/11
Type: Venture financing
Raised: €1.4 million ($2 million)
Investors: BioScience Ventures Group; V+ GmbH & Co. Fonds 3 KG; private investors

Verinata Health Inc., San Carlos, Calif.
Business: Diagnostic
Date completed: 8/9/11
Type: Venture financing
Raised: $48.5 million
Investors: Mohr Davidow Ventures; Sutter Hill Ventures; Alloy Ventures

Yaupon Therapeutics Inc., Malvern, Pa.
Business: Cancer, Neurology
Date completed: 8/11/11
Type: Venture financing
Raised: $14.4 million
Investors: Vivo Ventures; Palo Alto Investors; Burrill; Aperture Venture Partners

Other Financial News

Affymax Inc. (NASDAQ:AFFY), Palo Alto, Calif.
Business: Hematology
Date announced: 8/8/11

Affymax filed a shelf registration covering the sale of up to $100 million of its securities. The company, which closed Friday at $4.51, has 35.6 million shares outstanding.

Cumberland Pharmaceuticals Inc. (NASDAQ:CPIX), Nashville, Tenn.
Business: Gastrointestinal, Neurology, Hepatic
Date announced: 8/4/11

Cumberland amended its senior revolving credit facility with Bank of America to increase the facility to $10 million from $6 million and to extend the expiration date to Dec. 31, 2014. The facility may be increased to $20 million upon certain conditions.

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Other Financial News,
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Medifocus Inc. (TSX-V:MFS; OTCQX:MDFZF), Vancouver, B.C.
Business: Cancer
Date announced: 8/5/11

Medifocus said the Ontario Securities Commission (OSC) issued a 15-day order prohibiting all trading of the company's securities, effective Aug. 4, after the biotech failed to file its annual financial statement and related filings for the fiscal year ended March 31 by the July 29 deadline. Medifocus said it expects to submit its annual financial statement and related filings on or before Aug. 19, after which the company expects the order to be revoked.

NPS Pharmaceuticals Inc. (NASDAQ:NPSP), Bedminster, N.J.
Business: Endocrine, Musculoskeletal, Gastrointestinal
Date announced: 8/3/11

NPS Pharmaceuticals filed a shelf registration covering the sale of up to $150 million of its securities. The company, which closed Friday at $7.11, has 86 million shares outstanding.

Pharmasset Inc. (NASDAQ:VRUS), Princeton, N.J.
Business: Infectious
Date announced: 8/9/11

Pharmasset's board declared a stock dividend to effect a 2-for-1 stock split. On Aug. 31, each shareholder of record as of Aug. 22 will receive one share for each held. The company, which closed Friday at $125.03 has 37.7 million shares outstanding.

Sigma-Aldrich Corp. (NASDAQ:SIAL), St. Louis, Mo.
Business: Supply/Service
Date announced: 8/10/11

Sigma-Aldrich will pay to shareholders of record as of Sept. 1 a quarterly dividend of $0.18 on Sept. 15. At June 30, Sigma-Aldrich had $663 million in cash. The company, which closed on Friday at $63.17, has 122.1 million shares outstanding.

Synta Pharmaceuticals Corp. (NASDAQ:SNTA), Lexington, Mass.
Business: Cancer, Autoimmune
Date announced: 8/4/11

Synta filed a shelf registration covering the sale of up to $150 million of its securities. The company, which closed Friday at $67.17 has 49.5 million shares outstanding.

Technology Development Accelerator Fund, Cambridge, Mass.
Business: Finance
Date announced: 8/12/11

Harvard University's Technology Development Accelerator Fund said it plans to raise an additional $20-$30 million. The fund, which was created in 2007, awards investigators through a grant-selection process for projects that could help bridge the gap between academic research and commercialization. The fund said it previously raised $10 million and already awarded $5.2 million in grants to 32 projects.

University of Oxford, Oxford, U.K.
Business: Finance
Date announced: 8/6/11

The university's Isis Innovation technology transfer company raised £500,000 ($821,800) in a first close of its Oxford Invention Fund. The fund will make up to 10 investments in Oxford technologies.