Plain talk about valuations

By Steve Edelson
Senior Writer

These days, to keep the average venture investor in the average private company happy, the average pre-money valuation of a company’s IPO has to be $200 million. On average, that has been the case in this window, where the average pre-money valuation is $209.5 million.

But appearances can be deceiving. Indeed, there is downward pressure on venture rounds in response to this window, and the reason is that averages don’t tell all.

The key is that a few high IPO valuations have pushed the average up. In reality, 20 of the IPOs in this window have gone public well below the $200 million pre-money threshold, while only 16 have been close to or above that figure.

The numbers also have gotten worse as the window has matured. Excluding the $157 million IPO from Eyetech Pharmaceuticals Inc. (EYET, New York, N.Y.), which had a pre-money valuation of $674.6 million and a post-money valuation of $831.6 million, the average pre-money valuation of companies that went public in the first half of the window (October 2003 to April 2004) was $194.7 million. The average post-money valuation in this period was $257.7 million.

Abingworth’s Jonathan MacQuitty noted that the first batch of IPOs in the window had high enough valuations that “everybody along the line could get paid off.”

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The second half of the window looks different. MacQuitty attributed the valuation compression to “a very small number of players that want to buy IPOs. They have a foot on the IPO valuation hose, which forces compression down the line — it backs up everything.”

Excluding the three companies with high valuations — Idenix Pharmaceuticals Inc. (IDIX, Cambridge, Mass.), MannKind Corp. (MNKD, Valencia, Calif.) and Theravance Inc. (THRX, South San Francisco, Calif.) — the average pre-money valuation in the second half of this window (May to the present) is $107 million and the average post-money valuation is $143.4 million. Indeed, since May, IDIX, MNKD and THRX are the only companies that have gone public above the magic number of $200 million pre-money.

“The IPO market is telling you companies are worth $100-$150 million pre-money,” said Christoph Westphal of Polaris.

The numbers can work for VCs, even when the IPO doesn’t reach the magic threshold, but it’s too late to find this out

See next page
after a big bolus of pre-public money has been dumped into a company. As an example of a story that worked, Westphal cited Momenta Pharmaceuticals Inc. (MNTA, Cambridge, Mass.), which is developing therapeutics based on complex sugars.

"Momenta raised a total of $30 million in venture equity and went public at a pre-money valuation of $120 million. That, in this environment, is a great private deal," Westphal said. "But deals where there was $100 million in venture money raised and they went out at $150 million pre-money are not good venture deals."

According to Westphal, the problem isn't so much price as the amount of money some of these companies raised just prior to going public.

"The good thing in this market is that people haven't been paying high prices. That hasn't been the problem in the last two to three years. What's been difficult is that the amount of money going into companies is high — so that's dictated the valuations," he said. "Before the IPO market opened in the spring, some companies went out and raised large mezzanine rounds. But valuations in the IPO market have been lower than expected and so has the amount of money raised on IPOs. So it's become harder and harder to raise mezzanine rounds."

As a result, MacQuity noted, "It's much harder for everybody to get paid — somebody's not going to do well."

The result is predictable: VCs work backward from what the public market is willing to pay to figure out what they need to pay in order to ensure a profit down the line (see "A CEO's Tale," A5). They also are looking carefully at what kinds of companies the public market is willing to buy. In this window, IPO candidates lacking a Phase III compound or a validating partnership can expect a pre-money valuation of $130 million and a post-money valuation of $174.2 million (see "U.S. IPO Valuations," A4).

The consensus among VCs polled by BioCentury is that the average post-money valuation for a company after its mezzanine round today is about $100 million. At the round before that, companies typically have post-money valuations of $55-$90 million. Given that companies are raising an average of $27 million in series B and C rounds this year, this puts pre-money valuations at $30-$60 million.

Going further back, series A rounds this year are averaging just over $10 million, with post-money valuations of $15-$20 million. This puts pre-money valuations below $10 million.

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Value compression

Opinions in the venture community are varied on where the brunt of the crunch is occurring.

A Pax's Lori Rafid finds that early stage investors are being hit hard.

"Ten years ago, the formula was that a startup would be valued at $5-$10 million pre-money. Then it would raise $10 million. About 18 months later it would raise $15 million at a 2x step-up. Another 18 months later it would raise maybe $10 million and go public at $100-$150 million pre-money," she said. "If you do a startup at $5-$10 million pre and it goes public with a post-money of $200 million, you make a lot of money and don't get too diluted because you participated in the step-up rounds."

Now, she said, some series A companies are getting step-ups of only 10-15%. As a result, early stage investors "aren't getting paid for the sweat equity placed in new companies."

Joseph Piper of Integra Ventures thinks that B round investors are getting squeezed. He estimated that the post-money valuation of a series A company is $20 million or less. This year, he puts the average take from a series B round at $25 million.

"Here's where it gets rough in the valuation game," Piper said. "The VCs putting up the $25 million in a B round don't want the company to have a post-money valuation of $50 million — that's a little rich for their blood because they don't see the light at the end of the tunnel."

Indeed, because companies rarely go public after a B round, Piper said these investors know that "a larger private round is coming up for their companies. Because mezzanine investors will probably want about a 2x on their investment, they're going to back their way into a valuation," typically working from the $200 million pre-money valuation of an IPO company.

Further downstream, Brian Halk of Domain Associates thinks that series C rounds are where the valuations can get hairy.

"A company that has an interesting idea and needs proof of concept — either a small study in humans or a study in animals if there's a predictive disease model — usually has a pre-money value of $5 million before its series A and has a post-money of $15 million," he said. "If the study works, the company will do a B round on a pre-money valuation of $25 million." The post-money valuation will be about $45 million.

Now comes the problem, Halk said. To get the same step-up between a C and B round as it got between the B and A rounds, the company's pre-money valuation before its series C financing needs to be about $70 million. "If the company is looking to raise $30 million in the C, it would end up with a post-money valuation of $100 million. People get uncomfortable with this."

For both B and C rounds, MPM Capital's Steven St. Peter thinks the key is to raise enough money to get to an important value-creating event, such as late-stage data or a pharma deal.

"Not many private companies raise money at a post-money valuation of $100 million or more," he said. "Some companies get squeezed if they did a B or C round and didn't raise enough money to get to a data event that will attract a pharma partner or let them go public. Next round, they're stuck trying to raise money against the $100 million mark."

Even further downstream, because of the choppy IPO market, Alex Zissou of Thomas McNerney & Partners said the firm "is not..."
a big believer in doing mezzanine rounds. Normally, you’d like a 50% step-up in value in less than a year to take the risk of a mezzanine round. Even if investors guess right and the IPO happens, the deal may get done below the proposed range and trade down from there.”

An added danger, Zisson said, is that “if a company can’t go public, the next round will be brutal. The premium likely won’t be achieved in another mezzanine round.”

Rafield agreed that mezzanine investing is a dicey proposition. “There’s not that big of a step-up at the mezzanine level. Given this, why shouldn’t you just buy at the IPO?” she argued.

Indeed, Tom Keelin, a managing partner at Keelin Reeds, said there’s a dearth of mezzanine investors in today’s market. Keelin Reeds is a consulting firm that focuses in part on financing strategy and asset valuation for small companies.

“There’s a need for mezzanine financiers,” he said. “Many companies, in their own mind, are ready to go public, but they may be told by their bankers that they’re not late-stage enough. These companies may have proof of concept in Phase Ila or Phase II, which is one of the largest value-creating events for a company,” but IPO investors are focused on companies that are even further downstream.

Stepping up to the plate

Although there’s a wide variety of opinions on where the valuation crunch is most strongly felt, most VCs concur that the two important features that improve a company’s chances of a step-up round are late-stage compounds and a significant partner.

Clearly, this has been shown to apply to the IPO market. The three companies in this window that received post-money valuations of more than $600 million — EYET, THRXX and IDIX — each offered investors at least one of these features.

In fact, THRXX and IDIX both came up short in their first attempts at going public in 2000 and 2002, respectively. But when they came back the second time, each had signed broad collaborations with pharma companies: THRXX has a deal with GlaxoSmithKline plc (LSE:GSK; GSK, London, U.K.), while IDIX is partnered with Novartis AG (NVS; SW: NOVN, Basel, Switzerland).

THRXX and IDIX also had clinical compounds. THRXX has two asthma products that have completed Phase Ila studies and an antibiotic in Phase II testing. IDIX’s lead compound, telbivudine, is in Phase III testing to treat chronic HBV, with an NDA submission expected in late 2005.

When EYET went public, it already had a large deal for its Macugen pegaptanib anti-VEGF aptamer with Pfizer Inc. (PFE, New York, N.Y.). EYET also had Phase II/III data in hand for the compound in wet age-related macular degeneration (AMD). An NDA for Macugen has a Dec. 17 PDUFA date.

“If you see a clear shot at an NDA, like with Eyetech, you do the deal,” said Atlas’ Jean-Francois Formela. “In asking what makes for a strong exit value, Eyetech gives you the answer: take

*‘If you’re a preclinical company with a good lead candidate and credible management and the ability to make more compounds, you’ll probably be priced as a series A company.’*

— Jean-Francois Formela of Atlas

out the clinical risk.”

Apax’s Rafield agreed that companies getting financed at a step-up are those that have “washed out the risk of the clinical development process and have compelling Phase IIb data. If you don’t have that data, investors are getting an enormous amount of comfort with a substantial corporate partner that will mitigate a company’s financial risk.”

**Flocks of early birds**

In the absence of big pharma validation and efficacy data, private companies face the prospect of raising money at a flat valuation — at best — if their most advanced compound is shelfed in animals or just starting human studies.

According to Formela, the valuation curve is “flat until a company has safety data in humans. Even if you’re a preclinical company with a good lead candidate and credible management and the ability to make more compounds, you’ll probably be priced as a series A company. Very few people will give you a valuation higher than $10 million.”

Formela thinks this could apply to a lot of companies, because private plays with minimal clinical risk are few and far between.

“Who would have thought that as a private investor you have to take out clinical risk to get a good value?” he said. “That’s a hell of a burden to take.”

Nevertheless, VCs are hardly ready to stop putting money into early stage companies. The reason they will keep investing is the same reason that public investors continue to buy IPOs: it’s often the only way to get a big piece of the action.

Thus, Chris Ehrlich of InterWest said that getting into a company early in its development is necessary to participate in future rounds.

“The formula for a successful public company is late stage products, good management and partners,” he said. “When these companies come up for their pre-public rounds, it’s very competitive. I’ve learned that if you’re not in these companies by the time the pre-public (i.e., mezzanine) financing comes up, unless you’re already in, you can’t get in. If you have a big fund and want to put money into the winners, you need to get in early.”

**Pre-baked syndicates**

So VCs have no choice but to concoct strategies to make the numbers work. This includes an increasing emphasis on investing as part of a multi-round syndicate from the outset, and having deep enough pockets to participate in later rounds. When this is the case, the investors have less sensitivity to the price of each round, since they’re all in the same boat.

“The main determinant of how easy it is now to do a later round is if the previous round was mostly an insider round, especially if it was heavily syndicated,” said Westphal. “As a result, the only way I’ll start a company today is if it’s broadly syndicated at the beginning. I will not start a company without at least two or three other venture guys standing beside me.”

Westphal thus is seeing less competition among VCs. “In this
In most cases, VCs agree that a pre-money IPO valuation of $200 million provides enough air space to support step-ups negotiated in private rounds. The average pre-money valuation for recent U.S. IPOs is $209.5 million. However, the average pre-money valuation drops to $168 million after removing Eyetech (EYET), Idenix (IDIX) and Theravance (THRX), the only three IPOs to have pre-money valuations above $400 million. $M; deals sorted chronologically.

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Total $7,541.7 $9,647.1
Avg $209.5 $268.0
Total (excl EYET, IDIX, THRX) $5,543.0 $7,328.7
Avg (excl EYET, IDIX, THRX) $168.0 $222.1

**Holding pattern**

In addition to forming early syndicates and having the wherewithal to invest in a company multiple times, many VCs aren't jumping ship as soon as a company goes public and its lockup expires. Indeed, most companies that went public in this window have been relatively unscathed when their shares came off lockup (see BioCentury, May 24 & Aug. 30).

Part of the reason is that many VCs no longer view IPOs as liquidity events. Instead, going public is seen as just another financing. Rafield noted that significant data and partnering events often occur after a company has gone public. Thus, she said, "the biggest step-ups in value can occur in the public market. This tells us that we have to hold longer in the public market."

Denise Pollard-Knight of Nomura Phase4 also thinks that "a lot of VCs are not really viewing the IPO as their exit. It's a way for companies to raise more capital and stop raising private money. Then, the VCs basically have to wait for the news flow to drive the price in the public setting."
Plain Talk About Valuations

A CEO’s tale

“We’re hearing of C rounds that are 80-90% down — the VCs are taking whatever the post-money was from the previous round and dividing by four.”

— Anonymous biotech CEO

By Karen Bernstein
Editor-in-Chief

As investors work their venture round calculations back from the valuations that the public equity markets are willing to pay, companies seeking to do later rounds are feeling the pain. This is one CEO’s story, though the tales that others could tell would be similar. The names have been omitted and one small detail changed to protect the innocent.

The company is looking to raise a C round of $35-$45 million and has been on the road for 14 months. After four months, the CEO had a term sheet in hand with $30 million in commitments and what he said was a reasonable valuation — 33% down from the previous round. The round had a new lead investor, a group of other new investors, plus all the old investors. The company still needed one more deep pocket investor, although the CEO was willing to close at $30 million.

But then things started to come unglued.

“We were a preclinical company,” he said. “The post-money valuation would have been about $65 million or so as a result of this round. That wasn’t sitting well with the new investors who were concerned that, because the company would need another funding round before going public, the ultimate pre-money valuation would exceed the $150-$250 million that public investors are currently willing to tolerate. Thus the new investors wanted to push the valuation of the C round down still more in order to guarantee the 3-4X return that they wanted.

“At the same time, while some of the earlier investors were not sensitive to the valuation, others were unhappy that it wasn’t higher than $65 million.”

All this was better than many companies are getting, the CEO noted. “We’re hearing of C rounds that are 80-90% down — the VCs are taking whatever the post-money was from the previous round and dividing by four. We know one company that went through the same thing as us last year and had to lay off half their staff.”

The deal then fell apart due to issues that were unrelated to the company. However, the fundraising problems weren’t atypical.

“We were expecting the deal to close, we were spending at the existing rate because we had a goal of filing an IND by year end,” the CEO said. “When the deal fell apart, we were back to square one. We got a six-month bridge financing from our existing investors.”

Now, a few new investors who had said they weren’t interested are taking a second look, because they know the company is running up against a wall and that the valuation now will be still lower.

In this case, at least, the company hasn’t had to lay off any staff and still expects to get its IND filed. Other programs, however, have been back-burnered.

Information is everywhere...

Insight is not.


Strategy

Buying easy money

By Susan Schaeffer
Staff Writer

Last week’s acquisition of U.S. rights to Eli Lilly and Co.’s Vancocin Pulvules gives ViroPharma Inc. a jump forward from a Phase II company to one with a marketed drug. The company believes that by 2006, the product revenues will be sufficient to fund development of its pipeline going forward.

“Before, all the money we spent came from shareholders,” said Michel de Rosen, chairman, president and CEO. “Now, we have cash flow from Vancocin. We believe the money Vancocin generates will substantially fund our development by 2006.”


VPHM didn’t give sales guidance, but said 2004 U.S. revenue is expected to significantly exceed 2003 numbers. For the first half, it posted $28 million in sales.

Vancocin has averaged about 10% annual sales growth over the last 10 years with no promotion from LLY, according to VPHM, which believes it can continue to grow with a modest promotional effort.

“Anything they do is probably more than we have done,” said Joe Zakrzewski, LLY’s vice president of corporate business development. “Vancocin is one of the last infectious disease products that we market. We have been systematically getting out of the market and moving away from smaller drugs.”

According to VPHM, although Vancocin is the only drug approved by FDA to treat C. difficile-associated diarrhea (CDAD), it is held in reserve as a last resort, except in the most severe cases, because of concerns about the development of vancomycin-resistant strains. Metronidazole, though not approved for the indication, is generally used as first-line therapy. As a result, Vancocin is used in about 10% of the 600,000-750,000 patients with the disease, according to CSO Colin Bloom.

Joshua Tarnoff, vice president of commercial operations, also noted that metronidazole costs much less, at about $5 per course of therapy, compared to $200-$1,100 for Vancocin.

VPHM thinks it can address the resistance issue, and provide a value story as well.

For starters, VPHM believes that Vancocin’s contribution to resistance is likely to be negligible because the population for which the drug is indicated is small. More importantly, the company is conducting retrospective analyses of data it believes will show that when Vancocin is used earlier, it lowers morbidity and allows patients to be discharged from the hospital sooner.

Thus, while the company is not yet saying exactly how it will promote Vancocin, the plan will largely consist of producing the data that support earlier use and getting it into the hands of opinion leaders, possibly through a small team of medical science liaisons.

VPHM therefore will not create a sales force for Vancocin, and does not expect to spend more than $3 million per year on promotion. It expects gross margins, including distribution, will be greater than 80%.

While Vancocin has been off patent since 1996, VPHM said that there are no generics in the U.S. and only one in Europe. The company suggested additional generic competition is unlikely, because manufacturing of oral vancomycin is protected by trade secrets. Also, since Vancocin is not absorbed into the blood stream, establishing bioequivalence would likely require clinical trials.

VPHM also doesn’t expect near-term competition from other CDAD therapies in development. In August, Oscient Pharmaceuticals Corp. (OSCI, Wattham, Mass.) said its ramoplanin, while comparable to Vancocin, failed to demonstrate non-inferiority in a Phase II trial in CDAD (see BioCentury, Aug. 16).

Genzyme (GENZ, Cambridge, Mass.) also has its tolevamer in Phase II trials to treat CDAD.Unlike Vancocin, tolevamer works by binding toxins produced by C. difficile, rather than by acting on the bacteria directly.

VPHM will pay LLY (Indianapolis, Ind.) $116 million up front, just under three times 2003 sales. The payment includes $53.5 million from existing cash reserves and $62.5 million in proceeds from last week’s sale of senior notes and warrants to institutional investors (see B13).

VPHM expects to have $45 million in cash at year end, and projects positive cash flow from operations in 2006. Prior to the deal, de Rosen said, the company had enough cash to last until early 2006.

VPHM will pay royalties only on sales that fall within a predefined band, which starts at $44-$48 million depending on the year, and ends at $65 million. In 2005, the companies share 50-50 any sales within the band, and from 2006 through 2011, LLY’s take will be 35%. VPHM retains all sales below and above the band.

LLY will manufacture and distribute the drug for the first 18 months, after which both steps will be transferred to third parties.

Vancocin revenues will be used to fund development of VPHM’s Maribavir for cytomegalovirus, for which Phase II data are expected in mid-2005, and two HCV compounds for hospitals and transplant centers. HCV-086 is in a dose-ranging Phase Ib study. An IND for HCV-796 is expected in December. VPHM licensed Maribavir from GlaxoSmithKline plc (LSE:GSK; GSK, London, U.K.) in November 2003. The HCV compounds are partnered with Wyle (WYE, Madison, N.J.).

“With Maribavir, we wanted to be commercial as soon as possible,” said de Rosen. “We now have five value drivers: one product on the market, one in the hands of Schering-Plough and three products in the pipeline.”

In August, VPHM (Exton, Penn.) licensed its inhaled pleconaril for the common cold to Schering-Plough Corp. (SGP, Kenilworth, N.J.), and sold its biodefense antiviral programs to Sigatechnologies Inc. (SIGA, New York, N.Y.).
For the third time in as many years, CuraGen Corp. has announced plans to restructure and refocus its activities in order to continue its transition to product development. The plan is to concentrate resources on moving its most advanced products through the clinic while relying on its mature genomics-based discovery engine to fill out the pipeline.

As CMO and Executive Vice President of R&D Timothy Shannon sees it, the multiple workforce reductions have not occurred as a result of any failures at CuraGen (CRGN, New Haven, Conn.). To the contrary, he argued, the cuts reflect the company’s step-wise evolution towards sustainability. “We’ve done just what we wanted to do in developing clinical compounds, but unfortunately this creates issues,” he said, “which requires different skill sets as our portfolio moves into the clinic.”

Shannon said the company realizes the market has put an increasing emphasis upon mid- and late-stage clinical compounds. “We’ve responded by putting considerable effort towards identifying our best products over the last two years,” he said. By reducing its headcount, the company has been able to keep moving downstream while keeping its burn rate in check (see “Tracking CuraGen”).

In March 2003, CRGN started a Phase I trial of CG53135 human fibroblast growth factor 20 (FGF-20) in cancer patients at risk for mucositis following chemotherapy. This marked the company’s first venture into the clinic with an internally discovered product. Phase I results are expected this year, around which time the company expects to start Phase II testing.

This year, CRGN obtained ex-European right to its second lead compound, PXD101, via a licensing deal with Topotarget A/S (Copenhagen, Denmark) (see BioCentury, June 14). Early next year, the companies will begin Phase II testing of the HDAC inhibitor for solid and hematological cancers. According to Shannon, CRGN’s near-term goals are to support these two Phase II programs. In parallel, the company will use its scientific assets and genomics capabilities to continue to bring targets into its two ongoing discovery collaborations.

CRGN’s partnership with Bayer AG (FSE:BAYG; BAY, Leverkusen, Germany) is aimed at identifying and optimizing small molecules to treat obesity and diabetes. “We’ve put a large number of targets into this deal and just now we’re starting to see some come out the back end,” said Shannon. The companies expect to enter the clinic by the first half of 2006. CRGN also is partnered with Abgenix Inc. (ABGX, Fremont, Calif.) to discover and develop 250 antibodies for metabolic diseases, cancer, inflammation and autoimmune diseases. The companies plan to begin clinical testing in the next 18 months, including a Phase I trial of CR002 for kidney inflammation by the end of 2004 and a Phase I trial of CR011 for metastatic melanoma in early 2006. — Michael Flanagan
**Online links this week**

Links to the following documents reside online at BioCentury's News Center at www.biocentury.com.

**Agricultural biotechnology**
USDA database identifying U.S. utility patents on inventions in biotechnology and changes in patent ownership due to mergers, acquisitions and spinoffs.

**CHMP**
Summary of actions taken at the October meeting of the Committee for Medicinal Products for Human Use.

**Electronic filing**
Presentation from CBER's Regulatory Affairs Professional Society on electronic submissions to FDA for regulatory approval.

**Influenza**
FDA's chronology of events leading to the influenza vaccine manufacturing shutdown at Chiron Corp. (CHIR).

**Manufacturing**
Announcement of Nov. 16 forum co-sponsored by the FDA and ISPE, the International Society for Pharmaceutical Engineering, on pharmaceutical manufacturing based on Process Analytical Technology (PAT).

**PDUFA**
BIO's comments to FDA regarding proposed amendments to the interpretation of PDUFA.

**Product Documentation**
— Avastin: CHMP positive opinion for Avastin bevacizumab to treat metastatic colon cancer, from Roche (SW X:RO C Z) and Genentech Inc. (DNA).

— Fendrix: CHMP positive opinion for Fendrix hepatitis B vaccine to prevent HBV infection, from GlaxoSmithKline plc (LSE:GSK; GSK).

— Osseo/Protelos: CHMP EPAR for Osseo strontium ranelate to treat osteoporosis to reduce the risk of vertebral and hip fractures, and for Protelos strontium ranelate to treat osteoporosis, from Les Laboratories Servier.

— Quintanrix: CHMP positive opinion for Quintanrix vaccine to prevent diphtheria, tetanus, pertussis, and hepatitis B caused by Haemophilus influenzae type b, from GlaxoSmithKline plc (LSE:GSK; GSK).

— Trisenox: COMP summary of positive opinion for Orphan Drug designation for Trisenox arsenic trioxide to treat acute promyelocytic leukemia (APL), from Cell Therapeutics Inc. (CTIC;N Merc:CTIC).

— Yondelis: COMP summary of positive opinion for Orphan Drug designation for Yondelis ecteinascidin to treat soft tissue sarcoma, from PharmaMar S.A.

— Zemaira: FDA warning letter concerning failure to provide risk information for Zemaira human alpha1-proteinase inhibitor for maintenance of alpha1-proteinase (Al-PI) deficiency and clinical evidence of emphysema, from sanof-aventis group (Euronext:SNY; SAN).

**BioCentury makes people think**
There is only one journal — BioCentury, the Bernstein Report on BioBusiness® — that is recognized by key decision makers as the best source of perspective, interpretation and analysis for top managers and investors in the biotech community.
About a year to the day since going public, drug delivery company Advancis Pharmaceutical Corp. lost its anchor partner in GlaxoSmithKline plc and more than 60% of its market value. AVNC is now hoping investors will wait until the first half of 2005 for data from its Phase III trial of a pulsatile once daily formulation of amoxicillin for proof that AVNC’s Pulsys technology is commercially viable.

AVNC and GSK (LSE:GSK; GSK, London, U.K.) were developing a Pulsys version of the pharma company’s Augmentin amoxicillin/clavulanate antibiotic. While GSK did not say exactly why it ended the 2003 deal to use Pulsys for internal development programs, AVNC President and CEO Edward Rudnic said the decision was not due to scientific or clinical issues related to the Pulsys technology. Augmentin went generic in 2003.

AVNC had received $8 million in upfront and milestone payments, and stood to receive up to $52 million in total pre-commercialization milestones, plus sales milestones of up to $50 million and royalties.

In its own amoxicillin program, AVNC’s double-blind, placebo-controlled non-inferiority trial in 500 patients with pharyngitis is comparing 775 mg of amoxicillin Pulsys once daily for seven days to 250 mg of penicillin four times daily for 10 days. The primary endpoint is bacterial eradication. The company believes it needs to run only the one Phase III trial, and expects to submit a 505(b)(2) application in the second half of 2005.

Rudnic said using penicillin as a comparator is consistent with FDA guidance, and he does not expect to run an additional trial comparing amoxicillin Pulsys to immediate release amoxicillin.

“We believe this will be a very powerful marketing message to doctors,” as amoxicillin is preferred for its effectiveness, safety, and general tolerability, Rudnic said.

The Pulsys technology is based on research showing that bacteria exposed to antibiotics in short repetitive bursts, or pulses, are eliminated more efficiently compared to immediate release antibiotics, and tend not to develop resistance. The technology reduces the amount of active drug in each dose as well as the total treatment duration, thus reducing antibiotic exposure.

For example, 775 mg of amoxicillin Pulsys for seven days equals about 5 g of drug, while regular amoxicillin therapy for pharyngitis is dosed at 500 mg three times daily for 10 days, for a total of 15 g of drug.

AVNC (Germantown, Md.) expects to start a Phase III trial of a sprinkle formulation of amoxicillin Pulsys in pediatric pharyngitis/laryngitis patients in early 2005. The company also plans to develop a new formulation of amoxicillin Pulsys for otitis media, which AVNC expects will require a Phase II study that is likely to begin next year.

Amoxicillin Pulsys is partnered with Par Pharmaceuticals Inc., a subsidiary of Pharmaceuticals Resources Inc. (PRX, Spring Valley, N.Y.) (see BioCentury, March 8).

However, AVNC said it would discontinue development of a non-Pulsys generic formulation of Biaxin clarithromycin from Abbott Laboratories (ABT, Abbott Park, Ill.), which also was partnered with PRX.

According to the company, the bioequivalence studies barely failed to meet necessary peak concentration levels, and AVNC might have pursued the program under other circumstances. But Rudnic said the cutback would save at least “several million dollars” and a significant amount of employee time that can be directed to Pulsys products.

AVNC will continue selling antibiotic Keflex cephalixin, which it licensed from Eli Lilly and Co. Inc. (LLY, Indianapolis, Ind.) (see BioCentury Extra, July 1). Third quarter sales were $1.1 million. LLY reported about $4 million in Keflex sales in 2003.

AVNC is developing a pulsatile formulation of Keflex, which is expected to start Phase I testing in early 2005. Keflex is currently dosed two to four times daily for 7-14 days. In the meantime, AVNC believes an amoxicillin/clavulanate Pulsys compound is still worth pursuing. Rudnic noted that the company would prefer to have a partner to share development costs.

At Sept. 30, AVNC had $36.5 million in cash; the net loss for the quarter was $9.2 million. The company expects to end the year with $25-$27 million (see Ebb & Flow, A9).
**Product Development**

Roche’s HDL play

Roche’s deal for JTT-705 puts the phospholipid transfer protein and lecithin-cholesterol acyltransferase were unaffected. No toxicities were observed, but the highest dose of JTT-705 was associated with a non-significant increase in gastrointestinal side effects (p=0.058).

Pfizer (PFE, New York, N.Y.) has shown that its torcetrapib (CP-529,414) CETP inhibitor given alone or with Lipitor oratorvastatin significantly increased HDL in a single-blind Phase II trial in 19 subjects with low levels of HDL (see BioCentury, April 12). Torcetrapib is in Phase III, and Pfizer aims to seek marketing authorization in 2007.

Avant (AVAN, Needham, Mass.) reported preliminary Phase II results last year for its CETi-1 vaccine, which induces antibodies against CETP, showing a significant but small increase in HDL in a subset of patients (see BioCentury, Oct. 27, 2003). Avant is evaluating new adjuvants and delivery technologies for the vaccine and hopes to have a new CETP vaccine in the clinic by the end of 2005.

Roche is responsible for development of JTT-705 but has not disclosed a timeline or details on the indications it plans to pursue.

“There’s no real definition of the patients that we’re looking to address,” Taub said. “There are a lot of patients with metabolic syndrome. About 45% of our aging population has obesity, diabetes and/or high blood pressure. Many of these patients have a characteristic dyslipidemia associated with low HDL levels.”

— Christopher Maggos

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BioCentury makes people think

We know you have many choices for headlines. But if you need to know what the news means, there is only one journal — *BioCentury, The Bernstein Report on BioBusiness* — that is recognized by key decision makers as the best source of perspective, interpretation and analysis for top managers and investors in the biotech community.
Emerging Company Profile

Isogenica: Improving peptides

By Ludger Wess
Senior Editor

Although the possibility of using peptides as therapeutics is attractive, they still have disadvantages versus antibodies and small molecules. Isogenica Ltd. believes its Cis-display technology can improve the therapeutic properties of peptides, making them at least as attractive as monoclonal antibodies.

Compared to antibodies, peptides have lower production costs, greater stability and better interaction with the biologically active site of a target. However, antibodies have achieved superior affinity and specificity compared to peptides. And, in contrast to small molecules, peptides have poor in vivo stability and problems with oral delivery and cellular penetration.

Isogenica has set out to solve these problems with a technology that it claims can generate peptides with a specificity and affinity comparable to antibodies, as well as improved stability. The technology also is applicable to antibodies and is being expanded to generate large, diverse antibody libraries.

The company was spun out of Actinova Ltd., a subsidiary of Active Biotech AB (SSE:ACTI, Lund, Sweden), after ACTI decided to transfer all of its research activities back to Sweden in 2000 (see BioCentury, Jan. 31, 2000).

“Actinova had acquired Covalent Display Technology (CDT), a technology to link genes to their encoded polypeptides,” said Kevin FitzGerald, founder and CEO of Isogenica. “I started Isogenica to build a service play based on that technology.” The company later developed Cis-Display and doesn’t use CDT any more.

“Cis-Display is based on RepA, a replication initiation protein from bacteria,” FitzGerald said. “RepA binds exclusively to the template DNA from which it has been expressed. We have devised a method to genetically fuse peptide libraries to the N terminus of the RepA protein so that we achieve a direct linkage of peptides to the DNA molecules that encode them.”

Isogenica then uses a batch of randomly generated peptides with the DNA attached to screen against targets. “The binders can be varied and amplified using PCR,” he said. “This allows the rapid generation and screening of a huge number of compounds so that within a few rounds we achieve a much better affinity than with conventional evolutionary methods.”

FitzGerald added that Isogenica’s libraries are three to four orders of magnitude larger than the largest phage display libraries. “As it can all be done in vitro, it is a considerable advantage compared to phage display technologies where you have to insert libraries into bacterial cells first,” he said. “It is also much faster, with libraries generated within one day.”

The peptides have a length of 10-20 amino acids, and the company says it has produced ligands to enzymes like kinases and proteases, GPCRs, toxins and antibodies. According to FitzGerald, they show both the specificity and affinity of antibodies, reaching nanomolar inhibition.

The technology also can be used to make the peptides less unstable and more drug-like. “As an example, we can use non-natural peptides that can withstand the proteolytic activities of serum,” he said.

Isogenica also plans to address the antibody market, because antibodies right now are an “easier sell,” according to FitzGerald. “CIS display technology can be adapted to generate antibodies and should allow the creation of antibody libraries of unprecedented size and diversity, as it works very fast and entirely in vitro.”

In addition to generating revenues, Isogenica’s peptide discovery partnerships provide access to targets and biology expertise. In the long run, the company would like to form partnerships to develop peptide, antibody and protein drugs.

Isogenica is seeking to raise £2-£5 million ($3.6-$9 million) within six to nine months.
Washington Notebook

Political vaccine shortage

By Steve Usdin
Washington Editor

The convergence of the flu season with the electoral season means that it's open season to hurl invective at both FDA, a perennial whipping boy, and President Bush, who may or may not be available to kick around much longer.

Gunning for FDA

Some members of Congress are accusing FDA of a coverup, and collusion with drug companies, over data on an increased risk of suicidality among kids who take antidepressants. Members of Congress also are charging that FDA colluded with Merck to suppress warnings about Vioxx's cardiotoxicity. Finally, Congress is investigating the Chiron flu vaccine debacle. All in less than six weeks.

Flu politics

Focusing on the other end of Pennsylvania Avenue, the Kerry campaign is pushing the flu panic button. "George Bush and the Republicans are so busy bowing to drug companies, so busy giving them billions, helping them price gouge, pumping up their profits . . . so busy selling us out, they can't even get vaccines to keep pregnant woman safe from the flu," according to a Kerry radio ad aired in Florida last week.

The Democratic conditioner said the Bush administration "outsourced" flu vaccine to a foreign country (the U.K.). He also assailed the FDA, alleging it could and should have prevented the manufacturing problems at Chiron Corp. (CHIR, Emeryville, Calif.).

Kerry didn't mention that the U.S. has been obtaining flu vaccine from the same Liverpool plant since 1988. And while the candidate noted various reports have warned about the fragility of the vaccine supply chain for the last three years, he neglected to mention that scientific institutions have issued similar warnings for 20 years, none of which have prompted Democratic or Republican administrations or congresses to act.

Six out of 10 likely voters are "concerned" about the flu vaccine shortage, and 40% of senior citizens are "very concerned," according to an Oct. 17-19 ABC/Washington Post poll. So far, 27% "blame Bush."

Rep. Henry Waxman (D-Calif.) last week wrote Rep. Tom Davis (R-Va.), chair of the House Committee on Government Reform, urging him to subpoena documents from FDA about its oversight of the CHIR Liverpool facility.

"What is happening is obvious. The Administration is trying to delay the release of the vaccine documents until after the election," according to W axman.

Davis fired off a response expressing his satisfaction with FDA's explanation that it is too busy trying to secure additional doses. He noted that the agency is negotiating for vaccine with ID Biomedical Corp. (TSE:IDB; ID BE, Vancouver, B.C.), the French government, and GlaxoSmithKline plc (LSE:GSK; GSK, London, U.K.).

"Frankly, I am concerned that your push to subpoena the FDA is more about politics than fulfilling our oversight responsibility," Davis wrote.

Gray Lady does the math

The week began as The New York Times looked up north and came to a shocking revelation: Importation of drugs from Canada won't do much for Americans. In a weekend article, the Times noted: "To begin with, there are not enough Canadians, or drugs in Canada, to make much of a dent in the United States. There are 16 million American patients on Lipitor, for instance — more than half the entire Canadian population."

Flu vaccine & importation

Still, drug importation advocates are already accusing the FDA of hypocrisy for negotiating to import flu vaccine from Canada.

Acting FDA Commissioner Lester Crawford told reporters last week the vaccine situation "has no relevancy" to the reimportation debate. Crawford's argument centers on FDA's concerns that the chain of custody is broken under most importation arrangements: U.S. Customs has intercepted "Canadian" drugs that were actually from Africa or Asia.

In contrast, the vaccines will be "FDA-approved, under some sort of maybe abbreviated approval, but nonetheless, it will conform to U.S. standards," Crawford said. "And the exchange of the vaccine will be from the company that produced the vaccine and licensed it directly to the U.S. government. There will be no illegal shipments. There will be no concern about whether or not the Canadian government, for example, or the U.S. government has regulatory control over the product."

FOB tub-thumping

Even supporters of follow-on biologics jumped into the flu fray, seizing on the "abbreviated approval" idea for a biologic vaccine.

The Generic Pharmaceutical Association issued a statement asserting that the "flu vaccine shortage highlights America's critical need for biogenerics." According to GPHA, "generic alternatives would help stabilize the drug supply for critically needed drug products such as the flu vaccine in a market with limited players."

Association spokespersons, however, couldn't explain to BioCentury how a biogenerics pathway would have any impact on flu vaccine manufacturing.

BIO in transition

Amid the week’s bedlam, Rep. Jim Greenwood (R-Penn.) dropped by the Biotechnology Industry Organization to introduce himself to his future employees, but didn’t talk business. He’s precluded under House ethics rules from taking any part in decision making at BIO until his term expires during the first week of January, so the visit was limited to meet-and-greet.

Alan Eisenberg, formerly Greenwood’s legislative assistant for health and tax issues, started work at BIO last week as a special assistant to the president. He’s concentrating on the transition from the administration of Carl Feldbaum.
Ebb & Flow

AIMing low

By Shaun Brown & Steve Edelson
Senior Writers

A flurry of listings on AIM this month has been driven by a set of investors that differs significantly from investors in the types of biotech companies that would list on the main London market. While some of the latter investors have been indulging in hallway chatter that the AIM stories will draw money away from main market companies, there is no reason to believe that this would be the case. But the AIM flurry does point out the extent that value degradation has chiseled away at long-time public names in the U.K. and the Continent.

The money behind the AIM companies is mostly from small cap non-specialist investors and venture capital trusts, which invest in early stage lower risk companies for private investors. The later stage main list IPO candidates are regarded as higher risk and therefore mostly attract specialist investors.

“Among most AIM investors there is little specialist knowledge of biotech,” said Andy Smith of 3i. “The key is risk.”

For these investors, even a hint of revenues makes the AIM stocks appear to be lower risk bets than many of the better known main list names.

A mong this month’s AIM entrants, allergy vaccine company Allergy Therapeutics (LSE:AGY) recorded sales of £18 million ($32.3 million) and an operating profit of £1.6 million ($2.9 million) for the year ended June 30.

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The trial is expected to start next year.

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VASTox (LSE:VO X) had revenues of £250,000 ($450,000) from its drug discovery and toxicology services in the six months to June 30. And structure-based discovery play Sareum (LSE:SAR) recorded revenues of £21,000 ($37,663) for the 14 months to June 30 through its fee-for-service business.

Another anticipated listing on AIM is respiratory disease company Synairgen (LSE:SGN), which is expected to list on Tuesday with a market cap of about £28.2 million ($50.8 million). It raised £10 million ($18 million) in its IPO through the placing of 7.7 million shares at 130p.

SGN, which hasn’t disclosed any revenue, has preclinical programs for asthma and chronic obstructive pulmonary disease (COPD). The company also has a research deal with Merck (MRK) affiliate Merck Frosst in an undisclosed indication, and a fee-for-service deal with Cambridge Antibody Technology (LSE:CAT; CATG).

In valuation terms, SGN is just behind CeNes (LSE:CEN), an AIM listed name, which closed last week down 0.5p to 7.8p, giving it a market cap of £32 million ($57 million). Earlier this month, CEN raised £11.4 million ($22.5 million) to begin a second Phase III study of its lead product, M6G morphine-6-glucuronide metabolite of morphine to treat post-operative pain (see Ebb & Flow, Oct. 11).

Indeed, newly listed VOX could face profit-taking if investors start taking a look at relative valuations. Shares in the chemical genomics company have gained 51.5p (38%) to 186.5p since the company listed two weeks ago. The company had a market cap of £58 million ($105 million) on Friday on revenues of but £250,000 ($450,000) from its drug discovery and toxicology services in the six months to June 30.

The valuation is striking when compared to computational chemistry/biology and high throughput screening company Evotec OAI (FES: EVT), which closed Friday with a market cap of €111 million ($139 million) after saying it had lowered its 2004 revenue guidance to €70-€75 million ($87-94 million) (see below).

“There’s probably more bet placing on AIM biotech stocks and less rational investment decisions,” said John Goody of Deutsche Bank. “The risk with AIM stocks is that people speculatively bid them up and then run away.”

Thus specialists like 3i continue to put their money into U.K. main list stocks and U.S. companies. “We really don’t have a Medimmune, a Gilead, or a Cephalon. Many sophisticated U.K. investors would rather invest in the U.S. markets and these sorts of stories,” said Michelle Doig of Abingworth.

Doig feels the next window in the U.K. will be a cautious one that will lean towards companies with sales and earnings. “They are unlikely to be blockbuster companies. Rather they will be lower risk, lower reward companies,” she said.

ProStrakan is such a company, Doig noted. “It’s more in the niche specialty pharma area.” The drug delivery, endocrine and musculoskeletal company anticipates revenues this year of more than €30 million ($37 million) (see BioCentury, June 24).

Smith does not see ProStrakan looking to list this year, but when it does he expects the company would go to London’s main list. 3i is an investor in the stock.

Private rounds

Neurology drug reprofiler Vanda raised $37 million in a series B round. The company isn’t disclosing its milestones, but Chief Business Officer Chip Clark told Ebb & Flow that the funds should last through 2006.

Investors included Domain Associates; Prospect Venture Partners; Rho Ventures; MedImmune Ventures; Care Capital; and Bio*O ne Capital.

In Italy, BioXell raised €23 million ($28.7 million) in a series C round led by BB Biotech. Other investors in the genitourinary, endocrine and autoimmune company included NIF Ventures; Q ventures; MPM Capital; Index Ventures; AlpInvest Partners; Life Science Partners; and Investmenti Piccole Imprese.

Including the new round, BioXell has raised €63 million since it was spun out of Roche (SWX:ROC Z) in January 2002. The company will use the cash to run a Phase IIb trial of its BX L628 vitamin D3 analog to treat benign prostatic hyperplasia (BPH). The trial is expected to start next year.

See next page
BioXell also is developing vitamin D3 compounds with ProStrakan to treat osteoporosis and secondary hyperparathyroidism. The partners hope to identify a clinical candidate by year end.

From GAAP to gap

Gilead (GILD) dropped $3.43 to $33.25 on 17.6 million shares on Friday following earnings and pipeline news after market close on Thursday. On the earnings front, GILD reported GAAP EPS of $0.25, which beat the consensus estimates by $0.04. On the pipeline front, GILD terminated two clinical HIV compounds, which leaves the company's clinical cupboard with a single product (see "Gilead's Pipeline").

Putting downward pressure on the stock was a Friday downgrade to "sell" from "hold" by Legg Mason analyst Edward Nash, who said the EPS upside came mainly from lower-than-expected SG&A and R&D costs.

Nash predicted GILD will have to fill the pipeline gap “in the coming months” using cash and stock, but his firm has been “unable to identify any acquisition candidates for Gilead that would either be near-term accretive or fairly valued for acquisition” (see “Analyst Picks & Changes,” A15).

On the week, GILD was down $4.24 (11%) to $33.25.

Amgen’s new guidance plan

Amgen (AMGN) said on its quarterly conference call that it now plans to give 2005 guidance on its first quarter call, slated for late January. This will be the company’s plan for giving annual guidance going forward.

AMGN had been issuing guidance for the next year in December, but said reimbursement uncertainty was one reason to push out its forecast. Rather than predicting CMS’s decisions, “we are just going to have to wait and see what their ruling is and that’s one of the reasons that we’ve decided to wait until the end of January to chat with you all about ’05,” Chairman, President and CEO Kevin Sharer said on the call.

On the earnings side, AMGN reported EPS of $0.64, beating the Street’s $0.62 estimate by $0.02 and up 21% from EPS of $0.53 in the same period last year (see “EPS Watch,” A16). On the week, AMGN was down $2.52 to $52.70.

Whip-sawed

Celgene (CELG) dropped $6.01 (10%) to $56.12 last week, as shareholders had excuses to take profits on both good news and near-term uncertainties.

On Thursday, the stock lost $4.17 to $58.22 on 3.9 million shares despite the fact that third quarter EPS beat Street estimates. Company spokesperson Brian Gill attributed the selloff to a variety of factors. First, some investors sold on the good earnings news — the company had hit a 52-week high of $63.75 on Thursday, before the call.

Also, it’s possible that investors sold because of uncertainty on the action that FDA was likely to take at the Oct. 23 PDUFA date for CELG’s sNDA for Thalomid thalidomide to treat multiple myeloma (MM). Finally, some were selling on analyst reports that discussed the Thalomid uncertainty and the stock’s run-up.

The FDA jitters were resolved after market on Friday, when the company received an approvable letter for the sNDA. The letter said final data from the ECOG study in newly diagnosed MM patients could provide sufficient support for accelerated approval.

The sNDA included interim data from ECOG. CELG could have the data ready for submission in early 2005, which would restart a six-month approval clock and put potential approval out about nine months from now.

Chiron’s flu news

Although the media spilled a lot of ink on Chiron’s announcement on its earnings call that its ability to manufacture its Fluvirin flu vaccine for the 2005-06 flu season is not guaranteed, that tidbit wasn’t new news. Earlier this month, the company warned that its EPS queue

<table>
<thead>
<tr>
<th>Company</th>
<th>Date</th>
<th>Pre/post market</th>
<th>3Q04 EPS est</th>
<th>3Q03 EPS</th>
<th>Expected chg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Qiagen (FSE:QIA; QGENF)</td>
<td>10/25</td>
<td>post</td>
<td>$0.10</td>
<td>$0.08</td>
<td>25%</td>
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<tr>
<td>Serono (SWX:SEO; SRA)</td>
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<td>pre</td>
<td>$0.19</td>
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<td>12%</td>
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<tr>
<td>Biogen Idec (BIIB)</td>
<td>10/27</td>
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<td>$0.35</td>
<td>$0.26</td>
<td>35%</td>
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<tr>
<td>Charles River (CRL)</td>
<td>10/28</td>
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<td>$0.49</td>
<td>$0.40</td>
<td>23%</td>
</tr>
<tr>
<td>GlaxoSmithKline (LSE:GSK; GSK)</td>
<td>10/28</td>
<td>pre</td>
<td>$0.72</td>
<td>$0.66</td>
<td>9%</td>
</tr>
<tr>
<td>Invitrogen (IVGN)</td>
<td>10/28</td>
<td>post</td>
<td>$0.75</td>
<td>$0.57</td>
<td>32%</td>
</tr>
</tbody>
</table>

The earnings tide is ebbing, with about six profitable biotech and pharma companies slated to announce results this week. Last week saw the tidal wave, as 19 profitable companies reported their numbers (see “EPS Watch” A16).
ability to manufacture for the 2005-06 season may be compromised if its manufacturing suspension is not lifted by March 2005. What had come out of the call is that the 90-day suspension of CHIR’s license to manufacture FluVirin in the U.K. is due to expire on Jan. 3, 2005, and the company said it would not have anything more to say about future operations before that time.

CHIR, which announced earnings on Wednesday, was off $1.16 to $31.31 on the week.

**Fund watch**

Bioscience Managers set up the Maple Leaf Fund I for investments in Canadian mid-stage private life science companies. The investment manager will also consider PIPEs in Canada’s public life science companies and also will invest in M&A deals to bring international assets into Canada.

The fund’s only investor is Teachers’ Private Capital, the private equity arm of the C$79 billion ($63 billion) Ontario Teachers’ Pension Plan. “Effectively the fund has no ceiling. We look for good deals, and when we fund them,” Michael Forer, managing director of BML, told Ebb & Flow.

The team will focus on leading three or four investments over the next 24 months in series C or D rounds of C$20-$30 million ($16-$24 million). The Maple Leaf Fund will look to invest C$5-$10 million ($4-$8 million) in each round.

Teacher’s also is going to invest in BML BioEquity I, which will co-invest in European private therapeutic product companies, and other life science sectors (see Ebb & Flow, April 28, 2003). The other cornerstone investor in BioEquity I is expected to be Scottish Widows Investment Partnership. Scuttlebutt suggests the pan-

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**Analyst picks & changes**

<table>
<thead>
<tr>
<th>Company</th>
<th>Bank</th>
<th>Analyst</th>
<th>Coverage</th>
<th>Opinion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amgen (AMGN)</td>
<td>Friedman Billings</td>
<td>Ramsey</td>
<td>Jim</td>
<td>Downgrade</td>
</tr>
<tr>
<td>Antigenics (AGEN)</td>
<td>Needham</td>
<td>Mark Monane</td>
<td>Downgrade</td>
<td>Underperform (from hold)</td>
</tr>
<tr>
<td>Genzyme (GENZ)</td>
<td>Citigroup</td>
<td>Yaron Werber</td>
<td>Other</td>
<td>Hold</td>
</tr>
<tr>
<td>Gilead (GILD)</td>
<td>Legg Mason</td>
<td>Edward Nash</td>
<td>Downgrade</td>
<td>Sell (from hold)</td>
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<td>Metabasis (MBRX)</td>
<td>Legg Mason</td>
<td>Edward Nash</td>
<td>New</td>
<td>Hold</td>
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<tr>
<td>Myogen (MYOG)</td>
<td>Lazard</td>
<td>Gene Mack</td>
<td>Upgrade</td>
<td>Buy (from hold)</td>
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<tr>
<td>Neurocrine (NBIX)</td>
<td>C.E. Unterberg, Towbin</td>
<td>Matthew Osborne</td>
<td>New</td>
<td>Market perform</td>
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<tr>
<td>Osclent (OSCI)</td>
<td>JMP Securities</td>
<td>Adam Cutler</td>
<td>New</td>
<td>Strong buy</td>
</tr>
<tr>
<td>Protein Design (PDLI)</td>
<td>JMP Securities</td>
<td>Charles Duncan</td>
<td>Price target</td>
<td>Market outperform</td>
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<td>Sonus (SNUS)</td>
<td>Punk</td>
<td>Matthew Kaplan</td>
<td>Downgrade</td>
<td>Accumulate (from buy)</td>
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<tr>
<td>Teche (TECH)</td>
<td>Pacific Growth</td>
<td>Adam Chazan</td>
<td>Other</td>
<td>Equal weight</td>
</tr>
</tbody>
</table>

Reddoch thinks that Medicare reimbursement changes next year will prompt cancer patients to receive certain treatments in the hospital rather than at a clinic. As a result, he lowered his 2005 sales estimates for cancer anemia drug Aranesp to $2.9 billion from $3.12 billion and for cancer neutropenia drug Neulasta to $2.07 billion from $2.22 billion. AMGN closed Friday at $52.70, down $2.52 on the week.

Monane believes the company will need to run a second Phase III trial of Oncophage to treat renal cell cancer (RCC). AGEN closed Friday at $5.55, down $0.18 on the week.

Werber raised his 2004 and 2005 EPS estimates to $1.78 and $2.10 from $1.76 and $2.05, respectively. Last week, GENZ reported third quarter EPS $0.49, which beat the consensus estimate by $0.04. Werber expects the stock to continue to trade at a discount to other large-cap biotechs.

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Ebb & Flow,
from previous page

European fund is expected to close around year end at €150 million ($187 million).

Venture tracks

Steven Ratoff joined ProQuest Investments as a venture partner. Previously, he was senior vice president and CFO of the pharmaceutical group of Bristol-Myers (BMY). ProQuest has more than $350 million under management.

Regulatory milestones

Dyax (DYAX) plunged $1.99 (25%) to $6.08 on 2.4 million shares on Friday after news that it doesn’t expect to submit a BLA for its DX-88 to treat hereditary angioedema until after 2005. Following discussions with FDA, DYAX and partner Genzyme (GENZ) are planning additional clinical work that will be required for the submission. On a conference call, DYAX also said it still believes it will be the first to market for the indication. In September, Jerini began a Phase III trial of Icatibant to treat HAE. On the week, DYAX was off $2.01 (25%) to $6.08.

Neurocrine (NBIX) fell $2.70 to $44.28 on the week after submitting an NDA for the immediate-release formulation of its Indiplon to treat insomnia (see B8). Next month the company plans to seek approval for a modified-release formulation of the compound. Indiplon is partnered with Pfizer (PFE).

Advanced Magnetics (AVM) popped $2.88 (23%) to $15.15 on Tuesday and partner CytoGen (CYTO) advanced $2.01 to $10.58 after they submitted a complete response to a 2000 FDA approvable letter for Combidex to detect lymph node metastases. The MRI contrast agent has a PDUFA date of March 30, 2005.

AVM closed Friday at $14.38, up $2.08 (17%) on the week, but CYTO was off $0.27 to $9.96. On Thursday, CYTO said it expects 2004 revenues from imaging compounds Quadramet and Prostascint to grow 45-50% from a combined $9.8 million in 2003 sales. Previously, CYTO expected annual growth of 65-75%. The company said some sales territories are underperforming. Also, CYTO said it was experiencing delays in

See next page

<table>
<thead>
<tr>
<th>Company</th>
<th>3Q04 EPS est</th>
<th>3Q04 EPS actual</th>
<th>Outcome</th>
<th>Growth from 3Q03</th>
<th>10/22 eps cls</th>
<th>Wk `chg</th>
<th>% chg</th>
<th>Mcap chg</th>
<th>10/22 mcap</th>
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<tbody>
<tr>
<td>Affymetrix</td>
<td>$0.19</td>
<td>$0.25</td>
<td>Beat by $0.06</td>
<td>150%</td>
<td>$29.39</td>
<td>-$0.22</td>
<td>-1%</td>
<td>-$13</td>
<td>$1,780</td>
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<tr>
<td>Amgen</td>
<td>$0.62</td>
<td>$0.64</td>
<td>Beat by $0.02</td>
<td>21%</td>
<td>$52.70</td>
<td>-$2.52</td>
<td>-5%</td>
<td>-$3,205</td>
<td>$66,930</td>
</tr>
<tr>
<td>Celgene</td>
<td>$0.20</td>
<td>$0.24</td>
<td>Beat by $0.04</td>
<td>383%</td>
<td>$56.12</td>
<td>-$6.01</td>
<td>-10%</td>
<td>-$493</td>
<td>$4,604</td>
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<tr>
<td>Chiron</td>
<td>$0.06</td>
<td>$0.12</td>
<td>Beat by $0.06</td>
<td>-57%</td>
<td>$31.31</td>
<td>-$1.16</td>
<td>-4%</td>
<td>-$217</td>
<td>$5,866</td>
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<tr>
<td>Eli Lilly</td>
<td>$0.68</td>
<td>$0.69</td>
<td>Beat by $0.01</td>
<td>5%</td>
<td>$51.85</td>
<td>-$5.50</td>
<td>-10%</td>
<td>-$9,966</td>
<td>$56,247</td>
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<tr>
<td>Forest</td>
<td>$0.76</td>
<td>$0.79</td>
<td>Beat by $0.03</td>
<td>61%</td>
<td>$42.91</td>
<td>-$4.61</td>
<td>-10%</td>
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<td>Genzyme</td>
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<td>$0.49</td>
<td>Beat by $0.04</td>
<td>32%</td>
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<td>-1%</td>
<td>-$157</td>
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<tr>
<td>Gilead</td>
<td>$0.21</td>
<td>$0.25</td>
<td>Beat by $0.04</td>
<td>55%</td>
<td>$33.25</td>
<td>-$4.24</td>
<td>-11%</td>
<td>-$1,829</td>
<td>$14,340</td>
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<tr>
<td>AstraZeneca</td>
<td>$0.53</td>
<td>$0.55</td>
<td>Beat by $0.02</td>
<td>19%</td>
<td>$39.81</td>
<td>$1.58</td>
<td>4%</td>
<td>$2,637</td>
<td>$66,443</td>
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<tr>
<td>Amgen</td>
<td>$0.62</td>
<td>$0.64</td>
<td>Beat by $0.02</td>
<td>21%</td>
<td>$52.70</td>
<td>-$2.52</td>
<td>-5%</td>
<td>-$3,205</td>
<td>$66,930</td>
</tr>
</tbody>
</table>

Worldwide sales of cholesterol drug Crestor were $260M in 3Q04. The drug, approved in the U.S. last August, posted 3Q04 sales of $76M. AZN expects FY04 operating EPS of $2.10.

Celgene sales of Thalomid for erythema nodosum leprosum were up 36.7% quarter over quarter to $78.7M. For FY04, CELG increased its Thalomid revenue guidance to $305-$310M from $295-$305M. CELG also raised its FY04 EPS guidance to $0.60-$0.65 from $0.50-$0.60.

Chiron lowered all $91M of its Fluvirin inventory, which lowered 3Q04 EPS by $0.36. Product sales increased 23% quarter over quarter to $2.68 from $2.18. AMGN increased FY04 EPS and revenue guidance to $2.38-$2.43 from $2.30-$2.40 and to $10.3-$10.6B from $9.7-$10.4B.

Chirion bought back all $91M of its Fluvirin inventory, which lowered 3Q04 EPS by $0.36. 3Q04 sales of the flu vaccine were $103M. The company reiterated FY04 EPS guidance of $0.70-$0.80. Before CHIR’s Fluvirin manufacturing license was suspended, its FY04 EPS estimate was $1.80-$1.90.

Eli Lilly’s 3Q04 sales of erectile dysfunction drug Cialis were $154.1M, up 12% from $137.2M in 2Q04 and 207% more than $50.2M in 3Q03. Cialis tadalafil is marketed in North America and the EU by Lilly Icos, a joint venture between LLY and Icos (ICOS). Sales of depression drug Zyprexa fell 9% quarter over quarter to $1B from $1.1B. This shortfall in part prompted the company to cut 1,000 jobs.

Forest underperformed the major indexes over the week, with the Dow falling 6.6% and the S&P 500 down 7.0%. FRX pre-announced strong earnings earlier this month, at which time the Street was expecting 3Q04 EPS of $0.63. For fiscal 05, FRX expects EPS of at least $2.70.

Genzyme’s 3Q04 therapeutic revenues were $282.4M, up 27% from $222.6M in 3Q03. GENZ reiterated FY04 EPS guidance of $1.65-$1.75.

Gilead’s 3Q04 Truvada sales were $18.2M. Combined HIV product sales were $228.1M in 3Q04, up 88% from $121.4M in 3Q03. The increase in part reflects the August FDA approval and U.S. launch of HIV combination drug Truvada. 3Q04 Truvada sales were $18.2M.

See next page
3Q04 Growth
EPS EPS from 10/22 Wk % Mcap 10/22
Company est actual Outcome 3Q03 cls `chg chg mcap

Medicines Co. (MDCO) $0.05 $0.11 Beat by $0.06 NA  $24.73 $1.08 5% $52 $1,184

In 3Q03, MDCO reported a loss per share of $0.13. MDCO raised its FY04 revenue guidance to $139-$145M from $134-$139M. It raised the low end of its FY04 earnings guidance to $15M from $12M. The top end remains $19M.

MedImmune (MEDI) -$0.21 -$0.22 Missed by $0.01 NA  $26.34 $0.02 0% $5 $6,555

3Q04 sales were up 12% to $92M from $82M in 3Q03. MEDI for the first time gave 4Q04 revenue and EPS guidance of $435-$475M and $0.14-$0.18. The company also trimmed its FY04 revenue guidance to $1.11-$1.15B from $1.12-$1.16B and gave FY04 EPS guidance of $0.25-$0.29.

Merck (MRK) $0.71 $0.60 Missed by $0.11 -14%  $30.56 $0.06 0% $134 $68,033

3Q04 EPS included an $0.25 "unfavorable effect" associated with the global withdrawal of Vioxx rofecoxib. MRK expects 4Q04 EPS of $0.48-$0.53 and FY04 EPS of $2.59-$2.64.

Novartis (N VS; SW X:NO VN) NA $0.63 NA 21%  $46.96 $0.95 2% $2,319 $114,615

The two analysts who cover N VS and report to First Call had expected 3Q04 earnings per ADS of $0.57 and $0.59. For FY04, N VS reiterated that it expects to have high single-digit pharmaceutical sales growth.

Pfizer (PFE) $0.54 $0.55 Beat by $0.01 15%  $27.74 -$0.76 -3% -$5,738 $209,437

3Q04 human pharmaceutical sales were up 3% quarter over quarter to $11.3B. For the year, PFE expects EPS of $2.12-$2.14.

QLT (TSE:QLT; QLTI) $0.24 $0.25 Beat by $0.01 26%  $16.15 $0.30 2% $21 $1,124

3Q04 revenues were up 22% to $47M from $38.3M in 3Q03. The growth reflects strong sales of Visudyne with partner Novartis (N VS; SW X:NO VN). The AMD drug posted 3Q04 sales of $114M, up 27% from $89.9M in 3Q03. QLT increased the low end of its FY04 Visudyne sales guidance to $435M from $430M. The top end is still $455M.

sanofi-aventis (Euronext:SAN; SN Y) NA NA NA NA $35.64 -$0.31 -1% -$456 $52,391

The company, which is the result of the acquisition of Aventis by Sanofi, for the first time reported pro-forma figures. Pro forma 3Q04 pharmaceutical net sales were up 11% to €5.9B ($7.4B).

Schering-Plough (SGP) -$0.01 $0.01 Beat by $0.02 NA  $17.27 $0.11 1% $162 $25,412

3Q04 prescription pharmaceutical sales were down 2% quarter over quarter to $1.6B.

Techne (TECH) (B) $0.35 $0.34 Missed by $0.01 13%  $35.66 -$1.27 -3% -$52 $1,468

IQ 05 sales were up 8% to $40.9M.

Wyeth (WYE) $0.70 $0.76 Beat by $0.06 17%  $36.88 $0.08 0% $107 $49,193

3Q04 pharmaceutical sales were up 13% quarter over quarter to $3.6B.

Clinical milestones

Eyetech (EYET) fell $2 to $41.30 on the week after reporting two-year data from two Phase II/III trials of Macugen to treat wet age-related macular degeneration. Patients receiving the VEGF aptamer for two years had significantly less three-line loss on an eye chart compared to patients who only received Macugen for one year. The compound, partnered with Pfizer (PFE), has a Dec 17 PDUFA date.

Concept (CORT) edged down $0.20 to $7 on the week after starting a second Phase III trial of its Corlux mifepristone (C-1073) to treat the psychotic features of psychotic major depression (see B11). The company started the first Phase III trial in August. The trials have SPAs and CORT expects data in the first half of 2006.

deCode (DCGN) was up $0.54 to $7.27 on the week after releasing Phase IIa data showing that DG031, a 5-lipoxygenase activating protein (FLAP) inhibitor to prevent myocardial infarction, met the primary endpoint of suppressing production of three biomarkers: leukotriene B4 (LTB4), myeloperoxidase (MPO) and sICAM-1 (see B9). The company will meet with the FDA in November to discuss the results, and hopes to begin Phase III studies early next year.

Ebb & Flow

Advancis (AVNC) closed the week down $4.48 (63%) at $2.65 after plunging $4.53 (62%) to $2.75 on 2 million shares on Tuesday when partner GlaxoSmithKline (LSE:GSK; GSK) said it will end their deal to develop Augmentin amoxicillin/clavulanate antibiotics using AVNC's Pulsys drug delivery technology (see "Advancis Checks its Pulse," A9).

ViroPharma (VPHM) jumped $0.89 (43%) to $2.96 on the week after acquiring an approved antibiotic — Vancosin oral vancomycin capsules — to treat enterocolitis caused by Staphylococcus aureus and antibiotic-associated pseudomembranous
colitis caused by Clostridium difficile (see “Buying Easy Money,” A6).

Genaissance (GNSC) dropped $0.35 (13%) to $2.43 on Thursday after lowering its full year revenue guidance to $20-$21 million from $25 million. The genotyping specialist said the expected shortfall reflects the timing of contracts. Next year, GNSC hopes for revenue growth of more than 20%. On the week, GNSC was down $0.74 (25%) to $2.26.

London & the Continent

Evotec OAI (FSE:EVT) was off €0.71 (20%) to €2.89 on the week after lowering its revenue guidance for 2004 to €70-€75 million ($87-$94 million) against its previous guidance that 2004 would exceed 2003 revenues of €77.2 million. The company now expects negative EBITDA for 2004 of €4-€7 million ($5-$9 million) compared to a positive EBITDA of €4.1 million ($5.1 million) last year.

EVT said some long-term customers had shifted their budgets from preclinical discovery to clinical development and as a result scaled down or terminated discovery and development contracts. In addition, instrument deliveries have been affected by slower acquisition of new customers and introduction of new products. EVT’s market cap is €111 million ($139 million).

Pulmonary drug delivery company Vectura (LSE:VEC) gained 5p (10%) to 56p on the week after completing initial development of its GyroHaler dry powder asthma inhaler. The stock also may have been helped by scuttlebutt suggesting VEC and partner Arakis are in discussions to out-license AD 237, an inhaled muscarinic receptor antagonist to treat chronic obstructive pulmonary disease (COPD). The compound completed Phase IIa trials in May and is expected to enter Phase IIb by year end, with results in the first quarter of 2006. VEC has a market cap of €64 million ($116 million).

Regen (LSE:RGT) was up 0.1p to 3.25p on the week after acquiring a CRO, Guildford Clinical Pharmacology Unit, for £250,000 ($450,850) in stock (see B4). “The acquisition of the CRO makes sense as much of our expenditure is on CRO contracts,” said Percy Lomax, chairman and CEO of RGT. The company is developing Colostrinin, which is in Phase II trials to treat Alzheimer’s disease (AD). RGT has a market cap of £39 million ($16 million).
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 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.

TFCG Life Sciences Indexes
Weekly change in combined market capitalization. 12-week period. Tier I = market caps>$1B; Tier II <$1B. Base =100 on Dec. 31, 1998.

Price Gains
Stocks with greatest % price increase in the week ended Oct. 22. (Priced above $2.50; 25,000 minimum share volume)

<table>
<thead>
<tr>
<th>Company</th>
<th>Ticker</th>
<th>$Close</th>
<th>$Chg</th>
<th>%Chg</th>
<th>Vol(00)</th>
</tr>
</thead>
<tbody>
<tr>
<td>StemCells</td>
<td>STEM</td>
<td>2.700</td>
<td>0.880</td>
<td>48%</td>
<td>374062</td>
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<tr>
<td>ViroPharma</td>
<td>VPHM</td>
<td>2.960</td>
<td>0.890</td>
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<td>62849</td>
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<tr>
<td>Polydex</td>
<td>POLXF</td>
<td>6.680</td>
<td>1.480</td>
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<td>380</td>
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<td>21%</td>
<td>42572</td>
</tr>
<tr>
<td>Elan1</td>
<td>ELN</td>
<td>25.320</td>
<td>4.060</td>
<td>16%</td>
<td>393230</td>
</tr>
<tr>
<td>LifeCore</td>
<td>LCBM</td>
<td>9.900</td>
<td>1.440</td>
<td>17%</td>
<td>4609</td>
</tr>
<tr>
<td>Advanced Magenticss</td>
<td>AVM</td>
<td>14.380</td>
<td>2.080</td>
<td>17%</td>
<td>4117</td>
</tr>
<tr>
<td>New River</td>
<td>NRP</td>
<td>13.090</td>
<td>1.840</td>
<td>16%</td>
<td>2647</td>
</tr>
<tr>
<td>Oscient</td>
<td>OSCI</td>
<td>3.300</td>
<td>0.460</td>
<td>16%</td>
<td>19780</td>
</tr>
<tr>
<td>OraSure</td>
<td>OSUR</td>
<td>6.820</td>
<td>0.940</td>
<td>14%</td>
<td>47026</td>
</tr>
<tr>
<td>Genetronics</td>
<td>GEB</td>
<td>2.960</td>
<td>0.360</td>
<td>14%</td>
<td>3903</td>
</tr>
<tr>
<td>Idenix</td>
<td>IDIX</td>
<td>18.300</td>
<td>2.180</td>
<td>13%</td>
<td>4121</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Company</th>
<th>Ticker</th>
<th>$Close</th>
<th>$Chg</th>
<th>%Chg</th>
<th>Vol(00)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Advancis</td>
<td>AVNC</td>
<td>2.650</td>
<td>-4.480</td>
<td>-63%</td>
<td>31339</td>
</tr>
<tr>
<td>Dyax</td>
<td>DYA</td>
<td>6.080</td>
<td>-2.010</td>
<td>-25%</td>
<td>28052</td>
</tr>
<tr>
<td>Evotec</td>
<td>EVT</td>
<td>£2.890</td>
<td>-£0.710</td>
<td>-20%</td>
<td>18402</td>
</tr>
<tr>
<td>Cytokinetics</td>
<td>CYTK</td>
<td>8.910</td>
<td>-1.960</td>
<td>-18%</td>
<td>3553</td>
</tr>
<tr>
<td>Exact</td>
<td>EXAS</td>
<td>2.600</td>
<td>-0.530</td>
<td>-17%</td>
<td>27466</td>
</tr>
<tr>
<td>Salix</td>
<td>SLXP</td>
<td>15.000</td>
<td>-3.000</td>
<td>-17%</td>
<td>62645</td>
</tr>
<tr>
<td>NeoPharm</td>
<td>NEOL</td>
<td>6.480</td>
<td>-1.070</td>
<td>-14%</td>
<td>7093</td>
</tr>
<tr>
<td>Compugen</td>
<td>CGEN</td>
<td>3.780</td>
<td>-0.610</td>
<td>-14%</td>
<td>12933</td>
</tr>
<tr>
<td>Trinity1</td>
<td>TRIB</td>
<td>2.700</td>
<td>-0.420</td>
<td>-13%</td>
<td>358297</td>
</tr>
<tr>
<td>Curis</td>
<td>CRIS</td>
<td>3.250</td>
<td>-0.440</td>
<td>-12%</td>
<td>11781</td>
</tr>
<tr>
<td>Gilead</td>
<td>GILD</td>
<td>33.250</td>
<td>-4.240</td>
<td>-11%</td>
<td>3251</td>
</tr>
<tr>
<td>Phase Forward</td>
<td>PFW</td>
<td>7.150</td>
<td>-0.900</td>
<td>-11%</td>
<td>3251</td>
</tr>
<tr>
<td>Active Biotech</td>
<td>ACTIB</td>
<td>SEK39.1</td>
<td>-SEK4.9</td>
<td>-9%</td>
<td>3251</td>
</tr>
</tbody>
</table>

Volume Gains
Greatest changes in volume above 25,000 shares.

<table>
<thead>
<tr>
<th>Company</th>
<th>Ticker</th>
<th>Vol(00)</th>
<th>%Chg</th>
<th>$Close</th>
<th>$Chg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Advancis</td>
<td>AVNC</td>
<td>31339</td>
<td>540%</td>
<td>2.650</td>
<td>-4.480</td>
</tr>
<tr>
<td>ViroPharma</td>
<td>VPHM</td>
<td>62849</td>
<td>203%</td>
<td>2.960</td>
<td>0.890</td>
</tr>
<tr>
<td>Arena</td>
<td>ARNA</td>
<td>42572</td>
<td>95%</td>
<td>5.560</td>
<td>0.950</td>
</tr>
<tr>
<td>Polydex</td>
<td>POLXF</td>
<td>380</td>
<td>916%</td>
<td>6.680</td>
<td>1.480</td>
</tr>
<tr>
<td>LifeCell</td>
<td>LFC</td>
<td>62167</td>
<td>913%</td>
<td>9.000</td>
<td>-0.980</td>
</tr>
<tr>
<td>Genmab</td>
<td>GEN</td>
<td>10743</td>
<td>624%</td>
<td>DKK86.5</td>
<td>-DKK1.5</td>
</tr>
<tr>
<td>Advanced Magenticss</td>
<td>AVM</td>
<td>4117</td>
<td>593%</td>
<td>14.380</td>
<td>2.080</td>
</tr>
<tr>
<td>Evotec</td>
<td>EVT</td>
<td>18402</td>
<td>54%</td>
<td>£2.890</td>
<td>-£0.710</td>
</tr>
<tr>
<td>Inhibitex</td>
<td>INHX</td>
<td>7375</td>
<td>327%</td>
<td>5.910</td>
<td>0.390</td>
</tr>
<tr>
<td>Biocompatibles</td>
<td>BII</td>
<td>17375</td>
<td>301%</td>
<td>220p</td>
<td>-3.5p</td>
</tr>
<tr>
<td>Active Biotech</td>
<td>ACTIB</td>
<td>3251</td>
<td>288%</td>
<td>SEK39.1</td>
<td>-SEK4.9</td>
</tr>
<tr>
<td>Compugen</td>
<td>CGEN</td>
<td>2494</td>
<td>260%</td>
<td>3.780</td>
<td>-0.610</td>
</tr>
</tbody>
</table>

1 Volume figure is of ADSs (ADS = 1 share)

BioCentury 100 Advance-Decline Trend

<table>
<thead>
<tr>
<th>Week ended</th>
<th>BC100 Price level</th>
<th>BC100 Stocks gaining</th>
<th>BC100 Gaining vol. (00)</th>
<th>BC100 Declining vol. (00)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sep 24</td>
<td>1460.35</td>
<td>25</td>
<td>1228403</td>
<td>73</td>
</tr>
<tr>
<td>Oct 01</td>
<td>1485.31</td>
<td>68</td>
<td>2922401</td>
<td>30</td>
</tr>
<tr>
<td>Oct 08</td>
<td>1425.68</td>
<td>22</td>
<td>1178393</td>
<td>78</td>
</tr>
<tr>
<td>Oct 15</td>
<td>1414.77</td>
<td>22</td>
<td>923833</td>
<td>74</td>
</tr>
<tr>
<td>Oct 22</td>
<td>1392.13</td>
<td>33</td>
<td>1879812</td>
<td>67</td>
</tr>
</tbody>
</table>

Source: Thomson Financial

BioCentury tracks 492 issues that report prices and volume daily. The BioCentury 100 is a subset used to monitor price and volume trends. TFCG Life Sciences Indexes are compiled by Thomson Financial, provider of market intelligence services to publicly held companies.
Infectio Diagnostic B3
InnoCore B3
Insmed (INSM) B12
Integrated Bio (INB) B3
Inveresk (IRGI) B3
Invitrogen (IVGN) B4
Isis (ISIS) B2
Isogenica A11
Isotechnika (TSE:ISA) B6
Japan Tobacco A10, B4
Jerini A16
J&J (JNJ) B9
KAI Pharma B6
Kinexis B4
Kosan (KOSN) B7
Laboratories Servier A8
Liponex B10
MacroGenics B4
Mannkind (MNKD) A1
Max Plank B2
Maxim (MAXM; SSE:MAXM) B5,
MaxMira (MEDI) A13, B6, B12
Medical Discoveries (MLSC) B13
MedImmune (MEDI) A13, B6, B12
Merck (MRK) A13, B2, B3, B4,
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OCTOBER 25, 2004
October 25, 2004

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October 25, 2004

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‘It’s the BioCentury’

Authoritative. Globally focused. The leading perspective on the strategic issues essential to the formation, development and sustainability of life science ventures into 2005 and beyond.
More than 5 years ago, BioCentury, E.B.D. Group and BIO joined with our like-minded collaborators in the international banking and venture communities to launch Bio€quity Europe, a forum singularly focused on the financial health of European biotech.

Building on its growing successes in Munich, Frankfurt, Zurich, Paris, and Edinburgh, Bio€quity Europe returns to Zurich for its 6th anniversary event, offering an unparalleled showcase of investment opportunities at a critical time in the history of European life sciences.

Indeed, Bio€quity Europe 2005 will be perfectly timed. As Europe looks to widen the biotech investment window, the purpose of Bio€quity Europe is clearer than ever — to provide a unique, turf-neutral destination for life science companies, venture capitalists, asset managers and investment bankers to congregate and conduct business on a pan-European scale.

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Vontobel Investment Banking

**and Regional Host Committee Members**

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Greater Zurich Area  
Expanding business horizons

Bellevue Asset Management  
HBM BioVentures

**and Gold Equity Sponsor**

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Swiss Exchange  
Nomura
Using BioCentury Part II

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; Cancer; Cardiovascular; Chemistry; Combinatorial biology; Computational chemistry/biology; Dental; Dermatology; Diagnostic; Drug delivery; Endocrine; 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

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Biocon (NSE: BIOCONEQ)
Chiron (CHIR)
Chromatherap
Connetics (CNCT)
Diversa (DVSA)
Dor BioPharma (DOR)
GastroTech Pharma
GlycoMimetics
Hana Biosci
Isotechnika (Euronext: ISA)
KAI Pharma
Maxim (MAXM, SSE: MAXM)
Medimmune (MEDI)
Myriad (MYGN)
NeoRx (NERX)
Peregrine (PPHM)
Pharmion (PHRM)
Pozen (POZN)
Seattle Genetics (SGEN)
Synta
Theratechnologies (TSE: TH)
UCB (Euronext: UCB)
VaxGen (VXGN)
Vion (VIO)

Preclinical Results (Page B10)
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Aerovance
Aiteon (ALT)
BioSante (BPA)
Dynport
Edwards Lifesciences (EW)
Sangamo (SGMO)
N europharma

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Advant (AVAN)
BioCyst (BCRX)
Corcept (CORP)

See next page
**COMPANY NEWS/Deals, Sales & Marketing, Management Tracks**

### DEALS

**Alnylam Pharmaceuticals Inc.** (ALNY), Cambridge, Mass.

**Isis Pharmaceuticals Inc.** (ISIS), Carlsbad, Calif.

**Max Planck Society**, Munich, Germany

Business: Functional genomics

ALNY and ISIS co-exclusively licensed from the society certain IP relating to all therapeutic uses of microRNA (miRNA). The society’s Garching Innovation GmbH facilitated the transaction. MiRNA may play a role in regulating gene expression in mammalian cells, the companies said.

**Arena Pharmaceuticals Inc.** (ARNA), San Diego, Calif.

**Merck & Co. Inc.** (MRK), Whitehouse Station, N.J.

Business: Cardiovascular

The companies extended to October 2007 their 2002 deal for GPCR targets involved in cardiovascular disease (see BioCentury, Oct. 21, 2002). As extended, MRK will contribute $5.7 million in annual research funding for ARNA. Also, MRK invested $7.5 million in ARNA through the purchase of 938,000 shares at $8, a 74% premium to ARNA’s close of $4.61 on Oct. 19, the day before the extension was announced.

**Asinex Ltd.**, Moscow, Russia

**Recordati S.p.A.**, Milan, Italy

Business: Chemistry, Urology

Asinex will use its chemistry technologies to produce for Recordati a library of compounds to treat overactive bladder (OAB). Asinex also will synthesize the structures and provide lead optimization.

**Benitec Ltd.** (AXS-BLT), St. Lucia, Australia

**Panomics Inc.**, Redwood City, Calif.

Business: Genomics

BLT granted Panomics a worldwide, non-exclusive license to make and sell DNA-directed RNAi (ddRNAi)-based products. Panomics is developing tools for decoding the proteome, including arrays for global analysis of transcriptional regulation and cell signaling.

**Benitec Ltd.** (AXP-BLT), St. Lucia, Australia

**Stanford University**, Palo Alto, Calif.

Business: Functional genomics

BLT received an exclusive license from the university to use Minicircle DNA technology for all RNAi therapeutic uses. BLT also has sublicensing rights. The company said the technology allows for non-viral delivery of RNAi therapeutics.

**Biocon Ltd.** (NSE: BIO CON EQ), Bangalore, India

**Bioxell AG**

**Children’s Hospital & Research Center at Oakland**, Oakland, Calif.

Business: Infectious

BIOV received an exclusive option from the hospital to a vaccine candidate against Neisseria meningitides serogroup B, which causes meningitis. BIOV will provide the hospital with up to $800,000 in research funding for two years and will pay the hospital license fees, milestones and royalties.

**Cambrex Corp.** (CBM), East Rutherford, N.J.

**Genolife SA**, Saint Beaudrie, France

Business: Diagnostic

CBM subsidiary Cambrex France SARL acquired Genolife for about $6 million in cash. Genolife specializes in rapid microbial detection testing for the pharmaceutical, agriculture, food and cosmetic industries. CBM plans to incorporate Genolife’s technology with its endotoxin and mycoplasma detection product lines. The Genolife technology measures total viable organisms (TVO) in less than 5 hours rather than days or weeks required for other methods of detection, CBM said. CBM expects the acquisition to be neutral to EPS in 2005 and accretive thereafter.

**Celgene Corp.** (CELG), Warren, N.J.

**Penn Pharmaceutical**, Tredegar, U.K.

### Clinical Status, from previous page

Gilead (GILD)

Insmed (INSM)

Medimmune (MEDI)

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Sunesis

VaxGen (VXGN)

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Millennium (MLN)

Vitra Biosci/Bristol-Myers (BMY)

### FINANCIAL NEWS

**ViroPharma (VPHM)**

**Proposed Offerings (Page B13)**

**Zonagen (ZONA)**

**Other Financial News (Page B13)**

**BioProgress (AIM:BPRG; BPRG)**

**Bioscience Managers**

**Celgene (CELG)**

**NeoVacs**

Take advantage of BioCentury Extra.
Deals, from previous page

BioCentury Part II

Business: Cancer, Inflammation

CELG acquired Penn’s Penn T division for $110 million in cash. Penn T is the U.K. manufacturer of CELG’s Thalomid thalidomide, which is approved to treat erythema nodosum leprosum. CELG said the deal allows it to control manufacturing of Thalomid worldwide and is expected to be accretive by $0.05-$0.10 in 2005.

Charles River Laboratories International Inc. (CRL), W farms., Mass.

Inveresk Research Group Inc. (IRGI), Cary, N.C.

Business: Supply/Service

CRL completed its previously announced acquisition of IRGI, a CRO, in a stock and cash deal worth $1.5 billion based on CRL’s 0 ct. 19 closing price of $48.79. IRGI shareholders will receive 0.48 shares of CRL common stock and $15.15 in cash for each IRGI share, for a total of $38.53 per share. The acquisition was announced in July (see BioCentury, July 5).

Crucell N.V. (Euronext: CRXL; CRXL), Leiden, the Netherlands

Merck & Co. Inc. (MRK), W house Station, N.J.

Sanofi-Aventis S.A. (Euronext: SAN; SNY), Paris, France

Business: Veterinary

CRXL granted Merial Ltd. (London, U.K.), a JV between SAN and MRK, a license to use CRXL’s PER.C6 technology to develop and commercialize vaccines for foot-and-mouth disease (FMD). CRXL receives an upfront payment, annual maintenance fees, milestones and royalties. Merial is developing FMD vaccines discovered by the U.S. Department of Agriculture’s Agricultural Research Service (ARS). The vaccines will be held in reserve for emergencies.

Curis Inc. (CRIS), Cambridge, Mass.

Norak Biosciences Inc., Research Triangle, Park, N.C.

Business: High throughput screening

Norak will use its Transfluor G protein-coupled receptor (GPCR) technology to develop cell lines expressing selected receptors from CRIS. Financial terms were not disclosed. Norak licensed the Transfluor technology from Duke University (Durham, N.C.) in 1999.

Dade Behring Inc. (DADE), Deerfield, Ill.

University of Frankfurt, (DADE), Frankfurt, Germany

Business: Cardiovascular, Diagnostic

DADE received an exclusive worldwide license from the university to cardiac biomarkers relating to placental growth factor (PIGF) for cardiovascular diseases, and soluble CD40 ligand for prognosis of acute coronary syndrome (ACS).

Dynavax Technologies Corp. (DVAX), Berkeley, Calif.

Riken Institute, Tokyo, Japan

Business: Inflammation

The partners will develop therapies for cedar tree allergy. Under a two year deal, DVAX will supply its immunostimulatory sequence (ISS)-based allergy therapeutics to develop a cedar antigen-_ISS conjugate product. The institute will test therapeutic candidates in animal models of cedar polinosis.

Dynex Technologies Inc., Chantilly, Va.


Business: Supply/Service

Magellan acquired Dynex from parent company Capital Genomix Inc. (Gaithersburg, Md.) for an undisclosed sum. Dynex, which supplies microplate instrumentation, will operate as a subsidiary of Magellan. Magellan, which is majority owned by Ampersand Ventures, previously acquired tool company ESA Inc. (Helmsford, Md.).

Exelixis Inc. (EXEL), South San Francisco, Calif.

X-Ceptor Therapeutics Inc., San Diego, Calif.

Business: Metabolic, Cardiovascular

EXEL completed its planned acquisition of X-Ceptor for $2.9 million and 2.5 million shares. Using EXEL’s O ct. 18 close of $8.37, the shares are valued at $20.9 million and the total deal value is $23.8 million. X-Ceptor develops small molecules that target nuclear hormone receptors (NHRs) to treat metabolic and cardiovascular diseases. EXEL expects to file INDs by 2006 for X-Ceptor’s lead compounds that target the liver X receptor, farnesoid X receptor and mineralocorticoid receptor.

Genoa Sciences Inc. (GN SC), New Haven, Conn.

Pyxis Genomics Inc., Chicago, Ill.

Business: Agbio/Environmental, Genomics

GN SC will provide fee-for-service high-throughput genotyping for Pyxis’ Profile-1 System. The system includes a panel of SNPs, a search engine and a database for tracking animals and meat products throughout the production and distribution chain.

GeneOhm Sciences Inc., San Diego, Calif.

Infectio Diagnostic Inc., Sainte-Foy, Quebec

Business: Diagnostic

The companies plan to merge to form a molecular diagnostic company focused on infectious diseases. GeneOhm will bring its ePlex electrochemical detection technology, while Infectio has infectious disease assays for Group B Streptococcus (GBS) and methicillin resistant staph aureus (MRSA). The assays are approved in the U.S. and Canada. The company has an exclusive license from Cepheid Inc. (CPHD), Sunnyvale, Calif.) to distribute the Cepheid Smart Cycler platform for use with the assays. Financial details were not disclosed.

Genospectra Inc., Fremont, Calif.

Scripps Research Institute, La Jolla, Calif.

Business: Proteomics

Genospectra received an exclusive license from the institute to a patent estate covering state-responsive dyes used to create live-cell biosensors that can detect and quantify protein-protein interactions.

InnolCore Technologies BV, Groningen, the Netherlands

OctoPlus Technologies BV, Leiden, the Netherlands

Business: Drug delivery

Drug delivery company OctoPlus will collaborate with device and polymer company InnolCore to develop injectable, controlled-release polymer formulations of peptides and small molecules using InnolCore’s SynBiosys biodegradable polymeric system. OctoPlus is developing two other polymer delivery systems, PolylActive, a biodegradable polymeric drug delivery system for the controlled release of proteins and lipophilic small molecules, and OctoDEX, a dextran-based microsphere delivery technology for proteins and particulate systems.

Integrated BioPharma Inc. (IN B), Hillside, N.J.


Business: Infectious

IN B’s IN B Biotechnology Inc. subsidiary partnered with Fraunhofer to develop a plant production system for afluf vaccine. IN B’s technology uses transient expression vectors based on plant viruses.

See next page
Deals, from previous page

Kinexis Inc., Carlsbad, Calif.

Kinexis determined that prokineticin proteins modify the circadian rhythm in animal models, triggering an undisclosed milestone payment from MRK. Under a 2003 deal, the companies are working together to validate and screen small molecules against a prokineticin receptor target from Kinexis, for use in developing CNS therapeutics. Kinexis is eligible for additional milestones plus potential royalties.

MacroGenics Inc., Rockville, Md.

MacroGenics licensed exclusive rights to develop compounds against a cancer target from OriGene. MacroGenics will develop monoclonal antibodies to the target. OriGene is eligible to receive option fees, milestones and royalties.

MultiCell Technologies Inc. (MUCL), W arwick, R.I.

MultiCell will develop a bovine collagen matrix seeded with epidermal and dermal cells that will be used in the production of new skin treatments. The company will also develop a bovine collagen matrix for use in biomaterials.

Potomac Pharma Inc., Cabin John, Md.

Potomac will develop a bovine collagen matrix for use in the production of new skin treatments. The company will also develop a bovine collagen matrix for use in biomaterials.

Stanley Medical Research Institute, Bethesda, Md.

Stanley Medical Research Institute will invest $2.2 million in Potomac in the form of a convertible bond toward the development of P-101, an adrenergic receptor alpha 2 antagonist that is in Phase II trials to treat schizophrenia. The bond may convert into equity at a future date.

ReGen Therapeutics plc (LSE:RGT), London, U.K.

ReGen Therapeutics will develop a bovine collagen matrix for use in the production of new skin treatments. The company will also develop a bovine collagen matrix for use in biomaterials.

Response Biomedical Corp. (TSE:RBMB), Vancouver, B.C.

Response Biomedical Corp. will develop a bovine collagen matrix for use in the production of new skin treatments. The company will also develop a bovine collagen matrix for use in biomaterials.

Shionogi & Co. Ltd., Osaka, Japan

Shionogi will develop a bovine collagen matrix for use in the production of new skin treatments. The company will also develop a bovine collagen matrix for use in biomaterials.

Roche (SW X:RO CZ), Basel, Switzerland

Roche will develop a bovine collagen matrix for use in the production of new skin treatments. The company will also develop a bovine collagen matrix for use in biomaterials.

Japan Tobacco Inc., Tokyo, Japan

Japan Tobacco Inc. will develop a bovine collagen matrix for use in the production of new skin treatments. The company will also develop a bovine collagen matrix for use in biomaterials.
CYX’s Cambridge BioScience subsidiary received non-exclusive U.K. distribution rights to fluorescent labeling probes from IVGN’s Molecular Probes subsidiary. The deal has an initial term of two years.

OraSure Technologies Inc. (O SR), Bethlehem, Penn.
Business: Diagnostic
O SR launched in the U.S. O r a q u i c k A dv a n c e R a p i d H I V - 1 / 2 Antibody Test, which uses oral fluid, finger-stick or venipuncture whole blood or plasma samples to diagnose HIV.

Tm Bioscience Corp. (TSE:TMC), Toronto, Ontario
Business: Diagnostic
TMC launched an Ashkenazi Jewish Panel for its T a g - I t M u t a t i o n D e t e c t i o n K i t. The panel is used to detect 30 mutations that TMC said are associated with eight diseases.

OTHER NEWS

Amgen Inc. (AMGN), Thousand O ak s, Calif.
Transkaryotic Therapies Inc. (TKTX), Cambridge, Mass.
sanofi-aventis Group (Euronext:SAN ; S N Y), Paris, France
Business: Renal, Gene/Cell therapy
The U.K.’s House of Lords upheld a 2002 decision from the Court of Appeal that Dynepo epoetin delta from TKTX and Aventis, now SAN, did not infringe European patent No. 0 1 4 8 6 0 5 B 2 from AMGN covering erythropoietin (EPO). The Lords also reversed the Court of Appeal finding that the claims of AMGN’s patent were valid, stating, “It is clear that Amgen have got themselves into difficulties because, having invented a perfectly good and ground-breaking process for making EPO and its analogs, they were determined to try to patent the protein itself, notwithstanding that, even when isolated, it was not new,” said Lord Hoffman in the judgment.

TKTX said AMGN’s patent expires in mid-December. TKTX also said that if AMGN’s appeal had been successful, AMGN could have sought a post-expiry injunction to preclude manufacturing or selling Dynepo in the U.K. for the amount of time that the patent was judged to be infringed. In August, TKTX partnered with Lonza Ltd. (Basel, Switzerland) to manufacture Dynepo at its Slough, U.K., facility. TKTX expects to file an amendment to Dynepo’s product license in Europe in the third quarter of 2005 for the new manufacturing facility and plans to make Dynepo available in the EU in late 2005 or early 2006. Dynepo was approved in the EU in 2002.

Earlier this month, the U.S. District Court for the District of Massachusetts ruled that TKTX and AVE did infringe AMGN’s two process patents covering EPO. TKTX said it will appeal the ruling (see BioCentury, Oct. 21).

Angiotech Pharmaceuticals Inc. (TSE:ANP; AN PI), Vancouver, B.C.
Business: Drug delivery
AN P said it is planning to disclose on its N ov. 3 earnings call that it has started to consolidate its facilities, a task that will be spread out over the next year. The company said it has laid off about nine people at its Palo Alto, Calif., facility and will lay off a few more employees before year end. That facility, which the company acquired through its January 2003 purchase of Cohesion Technologies, previously employed about 35 people. Cohesion is focused on resorbable surgical hemostats and prevention of adhesions.

AN P plans to retain the eight or nine employees it has in Los Gatos, Calif., which it acquired when it bought N eu C o l l in August. N eu C o l l specializes in bone graft materials. AN P has not decided whether it will consolidate the two into a single location.

Curagen Corp. (CRGN), N ew H aven, Conn.
Business: Oncology, Inflammation, Metabolic
CRGN said it will cut its headcount by 110 to 240 to focus on advancing its clinical products and reducing its 2005 burn rate. The company said the cuts would mainly include employees supporting early R&D programs. The company plans to provide additional guidance during its Q 3, 2005 quarter financial conference call. As of June 30, CRGN had $375.1 million in cash and investments.

The company expects to start a Phase II trial of its CG53135 to prevent oral mucositis later this year, and a Phase II of PX D 101 to treat solid and hematological cancers in the first half of next year. CRGN also said that later this year it would start Phase I testing of its C R 0 0 2 to treat kidney inflammation.

In June 2003, CRGN reduced its headcount to 320 from 400 to shift resources from discovery-based processes to preclinical and clinical development (see BioCentury, June 23, 2003).

Genentech Inc. (D N A ), South San Francisco, Calif.
City of Hope National Medical Center, Duarte, Calif.
Business: Biopharmaceuticals
The California Court of Appeal upheld a 2002 jury ruling in the Los Angeles County Superior Court that DNA breached its contract and fiduciary duty with the medical center (see BioCentury, July 1, 2002). The jury ruled that DNA owes City of Hope compensatory damages of $300.2 million in royalties and awarded the City of Hope $200 million in punitive damages. DNA said it will seek to have the case reviewed by the California Supreme Court.

The litigation stems from a 1976 deal between the parties under which DNA agreed to fund recombinant DNA research at City of Hope in exchange for rights to file patent applications on resulting discoveries.

Maxim Pharmaceuticals Inc. (MAX M; SSE:MAX M), San Diego, Calif.
Business: Cancer, Infectious
MAX M said that it will cut its headcount by about 50% in an effort to reduce its burn rate after its Ceplene plus interleukin-2 (IL-2) failed a Phase III trial in advanced malignant melanoma patients last month.

MAX M said the restructuring will provide it with two years of funding. In the first half of 2005, the company plans to submit an N DA and MAA for Ceplene to treat acute myeloid leukemia (AML). Ceplene histamine dihydrochloride plus IL-2 has completed Phase III trials for AML and is under review in Europe to treat advanced malignant melanoma. MAX M, which reported an operating loss of $12 million for the second quarter, had $12.8 million in cash on June 30.

Pfizer Inc. (PFE), N ew York, N . Y.
sanofi-aventis Group (Euronext:SAN ; S N Y), Paris, France
Business: Endocrine
SAN said that PFE filed suit against it in the New York Supreme Court seeking a declaratory judgment that the acquisition of Aventis by Sanofi (through which SAN was formed) triggers a change of control provision in the companies’ deal to develop Exubera inhaled insulin. Aventis maintains that the provision has not been triggered and plans to respond to the complaint that PFE filed.

Under the deal, a change in control gives PFE the right to either sell its interest in the partnership to Aventis or buy Aventis’ interest. The
**Other News, from previous page**

sale or the purchase would be at fair-market value, as determined by investment banks appointed by the companies.

Exubera is in Phase III testing and uses delivery technology from Nektar Therapeutics (NKTR, San Carlos, Calif.).

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**MANAGEMENT TRACKS**

### Boards of Directors

**Biocon Ltd.** (NSE:BCON EQ), Bangalore, India
Business: Supply/Service
Appointed: Bala Manian, chairman and co-founder of Reametrix Inc., and co-founder of Q quantum Dot Corp. and Surromed Corp.

**Chiron Corp.** (CHIR), Emeryville, Calif.
Business: Biopharmaceuticals
Resigned: Richard Wills

**Gastrotech Pharma A/S**, Copenhagen, Denmark
Business: Gastrointestinal
Appointed: Tamas Bartfai, director of the Harold L. Dorris Neurological Research Center at The Scripps Research Institute

**Isotekhtika Inc.** (TSE:ISA), Edmonton, Alberta
Business: Autoimmune
Appointed: Patrice Debregeas, president, CEO and chairman of Ethypharm S.A.

**Pharmion Corp.** (PHRM), Boulder, Colo.
Business: Cancer
Appointed: Edward McKinley, a private investor
Retired: Jay Moorin

### Management

**Advancis Pharmaceutical Corp.** (AVNC), Germantown, Md.
Business: Drug delivery
Hired: Donald Anderson as VP of discovery, formerly global head of pharmacogenomics and clinical affairs at Aventis Pharmaceuticals Corp.

**Chroma Therapeutics Ltd.**, Oxford, U.K.
Business: Cancer
Hired: Richard Bungay as CFO, formerly director of corporate communications and strategic planning at Celltech Group plc; and Leon Hoofman as CMO, formerly head of clinical development at Celltech Group plc

**Connetics Corp.** (CNC), Palo Alto, Calif.
Business: Dermatology
Hired: Wendy Chern as VP of research and preclinical development, formerly head of early compound assessment and safety evaluation for the dermatology division of Aventis S.A.

**Diversa Corp.** (DVSA), San Diego, Calif.
Business: Combinatorial biology, Genomics, High throughput screening
Hired: Gary Noon as SVP of pharmaceuticals, formerly president of IMS Health U.S.

**Dor BioPharma Inc.** (DOR), Miami, Fla.
Business: Gastrointestinal
Hired: James Clavijo as controller, treasurer and corporate secretary, formerly finance manager at Wackenhut Corp.

**GlycoMimetics Inc.**, Gaithersburg, Md.
Business: Inflammation, Cancer
Hired: Colin Scott as VP of drug development, formerly VP of clinical and regulatory affairs at Arriva Pharmaceuticals Inc.

**Hana Biosciences Inc.**, South San Francisco, Calif.
Business: Cancer, Autoimmune
Hired: Gregory Berk as VP and CMO, formerly medical director for Network of Medical Communications and Research

**KAI Pharmaceuticals Inc.**, South San Francisco, Calif.
Business: Cardiovascular
Hired: Steven James as president and CEO, formerly SVP of commercial operations at Exelixis Inc.; he replaces John Walker, who remains a director

**MedImmune Inc.** (MEDI), Gaithersburg, Md.
Business: Biopharmaceuticals
Promoted: Edward Connor to EVP from SVP of clinical development, while remaining CMO; George Kemble to VP of viral vaccines R&D and general manager of MEDI's California facilities from senior director of research; and Dirk Reitsma to VP of clinical development for oncology from acting head of oncology
Hired: John Prunty to VP of finance and CFO from treasurer and controller

**Myriad Genetics Inc.** (MYGN), Salt Lake City, Utah
Business: Pharmacogenetics
Promoted: Edward Connors to EVP from SVP of clinical development, while remaining CMO; George Kemble to VP of viral vaccines R&D and general manager of MEDI's California facilities from senior director of research; and Dirk Reitsma to VP of clinical development for oncology from acting head of oncology
Hired: Mark Spring as VP of finance and controller, formerly VP of finance for the global renal division of Baxter International Inc.; and Sam Yonren as VP of product safety, formerly senior director and head of product safety and risk management at Millennium Pharmaceuticals Inc.

**NeoRx Corp.** (NERX), Seattle, Wash.
Business: Neurology
Hired: Susan Berland as CFO, formerly an industry consultant; and Caroline Loewy as VP of strategic development, formerly executive director of biotechnology equity research at Morgan Stanley Inc.

**Peregrine Pharmaceuticals Inc.** (PPHM), Tustin, Calif.
Business: Cancer
Appointed: Harold Dvorak, professor of pathology at Harvard Medical School

**Pozen Inc.** (POZN), Chapel Hill, N.C.
Business: Neurology
Hired: Marshall Reese as EVP of product development, formerly SVP and global head of R&D for consumer health care with Novartis Pharma AG

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*See next page*
Clinical activities and selected announcements for the week ended Oct. 22.

### REGULATORY

**Advanced Magnetics Inc.** (AVM), Cambridge, Mass.  
**Cytogen Corp.** (CYTO), Princeton, N.J.

**Product:** Combidex  
**Business:** Diagnostic

AVM submitted a complete response to a 2000 FDA approvable letter for Combidex magnetic resonance imaging contrast agent to detect lymph node metastases. The PDUFA date is March 30, 2005.

**Celgene Corp.** (CELG), Warren, N.J.

**Product:** Thalomid thalidomide  
**Business:** Cancer

CELG received an FDA approvable letter for an sNDA for Thalomid thalidomide to treat multiple myeloma (MM). The letter said that final data from the ECOG study in newly diagnosed MM patients could provide sufficient support for accelerated approval. The sNDA included interim data from that study.

CELG could have those data ready for submission in early 2005, which would restart a six-month approval clock and put potential approval out in about nine months from now.

**Genentech Inc.** (DNA), South San Francisco, Calif.  
**Roche** (SWX:ROCZ), Basel, Switzerland

**Product:** Avastin bevacizumab  
**Business:** Cancer

CHMP issued a positive opinion for an MAA for Avastin to treat metastatic carcinoma of the colon or rectum.

**GlaxoSmithKline plc** (GSK; LSE:GSK), London, U.K.

**Product:** Fendrix  
**Business:** Infectious

CHMP issued a positive opinion for an MAA for Fendrix hepatitis B recombinant DNA vaccine to prevent HBV infection in patients 15 years or older with renal insufficiency.

**Product:** Quintanrix  
**Business:** Infectious

CHMP issued a positive opinion for an MAA for Quintanrix for primary vaccination of infants and for booster vaccination of young children against diphtheria, tetanus, pertussis, HBV and invasive disease caused by Haemophilus influenzae type b (Hib).

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

**Product:** Ebixa  
**Business:** Neurology

EMEA received LUN’s filing for an extension of the indication for Ebixa to cover treatment of mild to moderate Alzheimer’s disease (AD). The oral NMDA receptor antagonist is approved to treat moderately-severe to severe AD in Europe and elsewhere.

**Kosan Biosciences Inc.** (KOSN), Hayward, Calif.

**Product:** 17-AAG  
**Business:** Cancer

FDA granted Orphan Drug designation to 17-AAG, an ansamycin antibiotic that binds to and inhibits hsp90, to treat multiple myeloma (MM). KOSN is in a Phase I trial for the same indication (see BioCentury, July 19).

**MedMira Inc.** (CDNX:MIR), Halifax, Nova Scotia

**Product:** Rapid HIV Test  
**Business:** Diagnostic

Health Canada granted marketing approval for the enhanced MedMira

**Seattle Genetics Inc.** (SGEN), Bothell, Wash.

**Hired:** Iqbal Grewal as VP of preclinical therapeutics, formerly senior scientist in immunology at Genentech Inc.

**Promoted:** Morris Rosenberg to SVP from VP of development; and Paul Carter to VP from senior director of antibody technologies

**Synta Pharmaceuticals Corp.** , Lexington, Ky.

**Hired:** Ninad Deshpanday as VP of drug product development, formerly technical business director for Cardinal Health Inc.’s pharmaceutics division

**Theratechnologies Inc.** (TSE:TH), Montreal, Quebec

**Hired:** Yves Rosconi as president and CEO, formerly SVP of Aventis Intercontinental Africa Middle East

**UCB Group** (Euronext:UCB), Brussels, Belgium

**Business:** Pharmaceuticals

**Promoted:** Luc Missorten to CFO from general manager of UCB Pharma Spain

**VaxGen Inc.** (VXGN), Brisbane, Calif.

**Business:** Infectious

**Hired:** Kathrin Jansen as SVP of R&D and CSO, formerly executive director of microbial vaccine research for Merck Research Laboratories

**Vion Pharmaceuticals Inc.** (VION), New Haven, Conn.

**Promoted:** Ann Cahill to VP of clinical development from senior director of clinical affairs

**Scientific Advisory Board**

**Alba Therapeutics Corp.** , Baltimore, Md.

**Business:** Autoimmune

**Appointed:** Richard DiMarchi, CEO of Ambrx Inc.; Roger Newton, CEO of Esperion Therapeutics Inc.; Gerald Galluppi, former director of investigative pharmacokinetics and drug metabolism at Pharmacia Corp.; and John Segartz, former head of global investigative toxicology at Pharmacia Corp.

**Hana Biosciences Inc.** , South San Francisco, Calif.

**Business:** Cancer, Autoimmune

**Appointed:** Robert Figlin, professor of medicine and urology and chair of urologic oncology at the UCLA School of Medicine
CLINICAL RESULTS

Aastrom Biosciences Inc. (ASTM), Ann Arbor, Mich.
Product: Tissue Repair Cells (TRCs)
Business: Musculoskeletal
Molecular target: NA
Description: TRCs made from bone marrow, containing adult stem cells using AastromReplicell System
Indication: Treat serious tibia fractures requiring bone graft
Endpoint: Graft repair on non-union tibial fracture
Status: Interim Phase III data
Milestone: Final Phase III data (2005)
Interim results from an open-label, Spanish Phase III trial in 5 patients showed that TRC treatment was safe and patients exhibited early stages of healing. ASTM plans to expand the study to enroll more patients.

Abbott Laboratories (ABT), Abbott Park, Ill.
Product: Humira adalimumab
Business: Autoimmune
Molecular target: Tumor necrosis factor (TNF) alpha
Description: Human monoclonal antibody against TNF alpha
Indication: Treat early rheumatoid arthritis (RA)
Endpoint: ACR50 response, inhibition of radiographic progression as measured by change in total Sharp score (TSS)
Status: Phase III data
Milestone: Submit NDA (year end 2004)

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Rapid HIV Test to detect HIV antibodies in human serum or plasma. MIR said the product will be made available immediately in Canada.

Neurocrine Biosciences Inc. (N BIX), San Diego, Calif.
Pfizer Inc. (PFE), New York, N.Y.
Product: Indiplon-IR
Business: N eurology
N BIX submitted an NDA for its indiplon immediate-release capsules to treat insomnia. The application contains data from 7 Phase III trials of the non-benzodiazepine GABA A receptor agonist in adult and elderly patients with transient and chronic insomnia. N BIX also is developing a modified release formulation, indiplon-MR, for which an NDA is expected to be submitted in November.
Pfizer Inc. (PFE), New York, N.Y.
Product: Vfend voriconazole
Business: Infectious
CHMP recommended label expansion for Vfend to treat candidiasis in non-neutropenic patients.

Schering-Plough Corp. (SGP), Kenilworth, N.J.
Product: Intron A interferon alpha-2b
Business: Infectious
CHMP recommended label expansions for Intron A/Viraferon interferon alfa-2b plus SGP’s Rebetol ribavirin, to treat HCV infection in children over age 3.

Serono S.A. (SW X :SEO ; SRA), Geneva, Switzerland
Product: Luveris
Business: Endocrine
FDA approved an NDA for Luveris, a recombinant human luteinizing hormone (LH), for concomitant use with SEO’s Gonal-f for stimulation of follicular development in infertile hypogonadotropic hypogonadal women with profound LH deficiency. The product has Orphan Drug designation in U.S.

Trimeris Inc. (TRMS), Durham, N.C.
Roche (SW X :RO C2), Basel, Switzerland
Product: Fuzeon enfuvirtide
Business: Infectious
FDA granted approval for Fuzeon, a viral fusion inhibitor peptide analog based on HIV gp41, to treat HIV infection.
Clinical Results, from previous page

BioSante Pharmaceuticals Inc. (BPA), Lincolnshire, Ill.
Product: Bio-E-Gel estradiol
Business: Endocrine
Molecular target: NA
Description: Bioidentical estradiol transdermal gel
Indication: Treat moderate to severe hot flashes caused by menopause
Endpoint: Reduction of hot flashes by >90% and >95%
Status: Phase II data
Milestone: N/A

In a 4-week, double-blind, placebo-controlled Phase II trial in 161 menopausal women, Bio-E-Gel gave a reduction in frequency of moderate to severe hot flashes by >90% in 55% of patients and by >95% in 50% of patients, compared to placebo (p<0.05). There was a 100% reduction in hot flashes in 24% of Bio-E-Gel patients compared to only 10% of placebo patients. There was a significant reduction in frequency and severity of hot flashes vs. baseline at all doses (p<0.001). The company said that enrollment is on schedule for a Bio-E-Gel Phase III trial (see BioCentury, Oct. 13, 2003). Results were presented at the American Society for Reproductive Medicine meeting in Philadelphia.

Bristol-Myers Squibb Co. (BMY), New York, N.Y.
Product: A batacept (CTLA4-1g)
Business: Autoimmune
Molecular target: NA
Description: CTLA4-Ig fusion protein
Indication: Treat rheumatoid arthritis (RA) in patients who did not adequately respond to methotrexate
Endpoint: Proportion of patients achieving an ACR 20 response at 6 months and progression of disease
Status: Phase III data
Milestone: Submit NDA (year end 2004)

In the double-blind, placebo-controlled Phase III AIM trial in 547 patients, 73.1% of patients given 10 mg/kg batacept IV treatment for 12 months, achieved an ACR 20 response vs. 39.7% on placebo (p<0.001). Data were presented at the American College of Rheumatology meeting in San Antonio.

Indication: Treat rheumatoid arthritis (RA) in patients who did not adequately respond to TNF inhibitors
Endpoint: Proportion of patients achieving an ACR 20 response at 6 months and progression of disease
Status: Phase III data
Milestone: Submit NDA (year end 2004)

In the double-blind Phase III ATTAIN trial in 391 patients, 50.4% of patients given 10 mg/kg batacept IV treatment for 6 months, achieved ACR 20 response vs. 19.5% on placebo (p<0.001). Data were presented at the American College of Rheumatology meeting in San Antonio.

deCode genetics Inc. (DCGN), Reykjavik, Iceland
Bayer AG (FSE:BAY Y; BAY), Leverkusen, Germany
Product: DG031
Business: Cardiovascular
Molecular target: 5-lipoxygenase
Description: 5-lipoxygenase activating protein (FLAP) inhibitor
Indication: Prevent heart attack in patients with history of heart attack and carry one or more at-risk gene variants
Endpoint: Reduction in heart attack-associated biomarkers
Status: Phase II data
Milestone: N/A

In a double-blind, placebo-controlled, dose-ranging, Icelandic Phase IIa trial in 172 patients, DG031 suppressed production of three biomarkers, leukotriene B4 (LTB4), myeloperoxidase (MPO) and sICAM-1, the primary endpoint.

Dong-A Pharmaceutical Co. Ltd. Seoul, South Korea
Product: DA-8159
Business: Genitourinary
Molecular target: Phosphodiesterase-5 (PDE-5)
Description: Highly selective phosphodiesterase-5(PDE-5) inhibitor
Indication: Treat erectile dysfunction (ED)
Endpoint: Change in the International Index of Erectile Function (IIEF) score after 12-weeks
Status: Phase II data
Milestone: N/A

In a double-blind, placebo-controlled Phase II trial in 319 men, 100 and 200 mg DA-8159 gave a higher change in IIEF score compared to placebo group (p<0.001), the primary endpoint. Data were presented at the World Congress of the International Society for Sexual and Impotence Research in Buenos Aires.

Encysive Pharmaceuticals Inc. (ENCY), Houston, Texas
Product: Thelin sitaxsentan
Business: Cardiovascular
Molecular target: Endothelin A receptor
Description: Endothelin A receptor antagonist
Indication: Treat pulmonary arterial hypertension (PAH)
Endpoint: Change in peak VO2 (average peak oxygen uptake during exercise) from baseline; improvement in six-minute walk (6MW) test, hemodynamics
Status: Phase II/III data
Milestone: N/A

Results from a double-blind, placebo-controlled sub-study of the Phase IIb/III ST RIDE-1 trial in 42 patients with PAH related to connective tissue disease showed a 58 meter improvement in the 6-minute walking distance for the Thelin group vs. placebo (p=0.0274). The difference in walk distance was due to a 20 meter increase in the Thelin group from baseline (p=0.0327) and a 38 meter decrease in the placebo group from baseline. Patients received either Thelin (100 or 300 mg) or placebo for 12 weeks. Data were presented at the American College of Rheumatology meeting in San Antonio.

Immunomedics Inc. (IMMU), Morris Plains, N. J.
Product: Epratuzumab (AMG 412)
Business: Autoimmune
Molecular target: CD22
Description: Humanized antibody targeting CD22
Indication: Treat systemic lupus erythematosus (SLE)
Endpoint: Not Disclosed
Status: Phase II data
Milestone: N/A

In a double-blind, placebo-controlled, dose-ranging, European Phase II trial, 9 of 14 patients had lowered global British Isles Lupus Assessment Group (BILAG) scores by at least 50%, 24 hours after therapy. Six of 7 patients who returned for a 6-month checkup retained clinical benefit. Results were presented at the American College of Rheumatology meeting in San Antonio.

Johnson & Johnson (JNJ), New Brunswick, N. J.
Schering-Plough Corp. (SGP), Kenilworth, N. J.
Product: Remicade infliximab
Business: Autoimmune
Molecular target: Tumor necrosis factor (TNF) alpha

See next page
Clinical Results, from previous page

Description: Chimeric monoclonal antibody against tumor necrosis factor (TNF) alpha
Indication: Treat ankylosing spondylitis
Endpoint: 20% or greater improvement in ankylosing spondylitis assessment (ASAS 20) at 24 weeks
Status: Phase III data
Milestone: NA

Data from a 24-week sub-analysis study of the double-blind, placebo-controlled, North American and European Phase III ASSERT trial in 266 evaluable patients showed that Remicade treatment gave a median decrease of 73% in spinal inflammation activity score compared to 0% in placebo group (p<0.001). Results were presented at the American College of Rheumatology meeting in San Antonio.

Indication: Treat early rheumatoid arthritis (RA)
Endpoint: Modified Sharp score, Health Assessment Questionnaire (HAQ)
Status: Phase III data
Milestone: NA

Data from a subset analysis of the ASPIRE study in 138 RA patients with no joint erosion showed that after one year of treatment, 79% of patients who received Remicade in combination with methotrexate had no new erosion compared to 58% patients receiving methotrexate only (p=0.012). The combination received FDA approval this month (see BioCentury Oct. 04). Data were presented at the American College of Rheumatology meeting in San Antonio.

Liponex Inc., Ottawa, Ontario
Product: CRD5
Business: Cardiovascular
Molecular target: NA
Description: Plasma lipid modifying drug using charge control technology
Indication: Treat cholesterol and atherosclerosis
Endpoint: Safety; determine the profiles of individual plasma lipoproteins and lipid levels after treatment with CRD5
Status: Phase I data
Milestone: Start Phase II (2005)

In a 2-week, Canadian Phase I trial in 56 volunteers, CRD5 was safe and well tolerated. Preliminary efficacy data showed CRD5 increased levels of HDL cholesterol by 18%. Also, LDL cholesterol and triglyceride levels decreased by 15% and 60%, respectively. The Phase I trial was designed to have 3 stages, where part Ia and Ib were open-label and IC was double-blind and placebo-controlled. Data were presented at the Canadian Lipoprotein Conference in Alberta.

Merck & Co. Inc. (MRK), W hitehouse Station, N. J.
Product: Arcoxia etoricoxib (MRK-663)
Business: Autoimmune
Molecular target: Cyclooxygenase-2 (COX-2)
Description: Cyclooxygenase-2 (COX-2) inhibitor
Indication: Treat chronic osteoarthritis (OA)
Endpoint: Gastrointestinal (GI) tolerability
Status: NA
Milestone: PDUFA date (10/30/04)

In the 1-year, double-blind, international EDGE study in 7,111 osteoarthritic patients, Arcoxia significantly reduced the rate of discontinuations due to GI adverse events by 50% compared to diclofenac sodium treatment (p<0.001). Data were presented at the American College of Rheumatology meeting in San Antonio.

PTC Therapeutics Inc., South Plainfield, N J.
Product: PTC124
Business: Musculoskeletal
Molecular target: NA
Description: Small molecule that facilitates complete translation of proteins containing nonsense mutations
Indication: Treat Duchenne muscular dystrophy and cystic fibrosis (CF) due to nonsense mutations
Endpoint: Safety and pharmacokinetics
Status: Preliminary Phase I data
Milestone: Final Phase I data (early 2005); start Phase II (2005)

Preliminary results from a dose-escalating Phase I trial in 16 healthy volunteers showed that PRC124 was orally bioavailable and was well tolerated. Data were presented at the North American Cystic Fibrosis Conference in St. Louis.

Savient Pharmaceuticals Inc. (SVNT), East Brunswick, N J
Product: Puricase
Business: Metabolic
Molecular target: NA
Description: Pegylated urate oxidase (uricase)
Indication: Treat refractory gout
Endpoint: Safety, tolerability, pharmacokinetics, uric acid levels
Status: Phase I data
Milestone: Complete Phase II (2004); start Phase III (2005)

In an open-label, U. S. Phase I trial in 13 patients, subcutaneous administration of Puricase resulted in injection-site reactions and drug intolerance in some patients. SVNT said this was not seen in the Puricase IV Phase I trial. Sustained reduction in plasma uric acid was seen in both trials. Data were presented at the American College of Rheumatology meeting in San Antonio.

Tap Pharmaceutical Products Inc., Lake Forest, Ill.
Product: Febuxostat
Business: Metabolic
Molecular target: Xanthine oxidase
Description: Non-purine selective inhibitor of xanthine oxidase
Indication: Treat chronic gout
Endpoint: Number of patients in each treatment group whose last three consecutive monthly serum uric acid (sUA) levels ≤6.0 mg/dL
Status: Phase III data
Milestone: NA

In a Phase III trial in 760 patients with sUA ≥8.0 mg/dL, 53% of patients given 80 mg Febuxostat and 62% given 120 mg Febuxostat achieved and maintained sUA <6 mg/dL, compared to 21% patients in the allopurinol group. Results were presented at the American College of Rheumatology meeting in San Antonio.

PRECLINICAL RESULTS

Aeolus Pharmaceuticals Inc. (AO LS), Research Triangle Park, N. C.
Product: AEO L 10150
Indication: Protect islet cells for transplantation in diabetic patients

Researchers published in Diabetes that prompt use of AEO L 10150 catalytic antioxidant with human pancreatic islet cells during isolation reduced cell loss, improved islet viability and metabolic function, and resulted in larger numbers of functional islets for transplantation in diabetic patients.

Aerovance Inc., Berkeley, Calif.
Product: AER-002
Indication: Treat cystic fibrosis (CF)

See next page
Preclinical Results, from previous page

In vitro analysis of bronchoalveolar lavage fluids from CF patients showed that AER-002 inhibited the activity of destructive enzymes that cause lung tissue degradation. Also, in Cynomolgus monkey model of CF, AER-002 could control salt regulation in lung. AER-002 (formerly Bikunin) is a recombinant protease inhibitor that blocks a sodium channel enzyme. Data were presented at the North American Cystic Fibrosis conference in St. Louis.

**Alteon Inc.** (ALT), Ramsey, N.J.
Product: Alagebrium (ALT-711)
Indication: Treat diabetic erectile dysfunction (ED)
In a rat model of diabetes with erectile dysfunction (ED), delayed administration of alagebrium improved ED compared to ALT’s aminoquinidine. Data were presented at the International Society for Sexual and Impotence Research meeting in Buenos Aires.

**BioSante Pharmaceuticals Inc.** (BPA), Lincolnshire, Ill.
**DynPort Vaccine Co., LLC**, Frederick, Md.
Product: Calcium phosphate nanoparticles (CAP)
Indication: Prevent anthrax infection
In a mouse model of anthrax, anthrax vaccine used with Bioviant adjuvant elicited immunity compared to a negative response from antigen alone or anthrax vaccine used with Alhydrogel adjuvant. Biovant nanotechnology-based vaccine adjuvant was used with Dynport’s recombinant anthrax antigens. Data were presented at the World Vaccine Congress in Lyon.

**Edwards Lifesciences Corp.** (EW), Irvine, Calif.
**Sangamo BioSciences Inc.** (SGMO), Richmond, Calif.
Product: EW-A-401
Indication: Treat peripheral artery disease (PAD)
Researchers published in Circulation that EW-A-401, a plasmid DNA that encodes a zinc-finger DNA binding protein transcription factor (ZFP TF), produced all forms of VEGF protein in the oxygen starved muscles in a rabbit model of PAD. The product significantly improved blood vessel growth and blood flow in the limbs.

**Neuropharma S.A.U.**, Madrid, Spain
Product: N P0361
Indication: Treat Alzheimer’s disease (AD)
In a transgenic mice model of AD, N P0361, a dual acetyl cholinesterase inhibitor, decreased amyloid plaque load in the brain and improved cognitive function. Data were presented at the Neuroscience and Impotence Research meeting in Buenos Aires.

**Avant Immunotherapeutics Inc.** (AVAN), Needham, Mass.
Product: TP10
Business: Cardiovascular
Molecular target: Complement 3 (C3); Complement 4b (C4b)
Description: Soluble complement receptor 1 (sCR1)
Indication: Prevent organ damage occurring in patients with cardiac surgery using cardiopulmonary bypass
Endpoint: Incidence of death or myocardial infarction (MI)
Status: Phase Ib/II ongoing
Milestone: Phase Ib/II data (1H05)
AVAN announced that its double-blind, placebo-controlled, U.S. Phase Ib/II trial in 300 female patients, originally to be completed by year end, will now be completed in the 1H05.

**BioCryst Pharmaceuticals Inc.** (BCRX), Birmingham, Ala.
Product: Forodesine hydrochloride (BCX-1777)
Business: Cancer
Molecular target: Purine nucleoside phosphorylase
Description: Purine nucleoside phosphorylase (PNP) inhibitor
Indication: Treat refractory cutaneous T cell lymphoma (CTCL)
Endpoint: Safety; pharmacokinetics
Status: Started Phase I
Milestone: Start Phase II (early 2005)
BCRX began an open-label, U.S. Phase I trial in about 50 patients who will receive 4 weeks of a once-daily dose of either 40, 80 or 160 mg/m² of Forodesine capsules. The product has an Orphan Drug designation in the U.S. for this indication (see BioCentury Aug. 30).

**Corcept Therapeutics Inc.** (CORT), Menlo Park, Calif.
Product: Corlux mifepristone
Business: Neurology
Molecular target: Progesterone receptor
Description: Small molecule antiprogestin
Indication: Treat psychotic major depression (PMD)
Endpoint: Proportion of patients with at least a 50% improvement in the Brief Psychiatric Rating Scale Positive Symptom Subscale (BPRS PSS) at days 7 and 56
Status: Started Phase III
Milestone: Interim Phase III data (1H06)
CORT began the double-blind, placebo-controlled, U.S. Phase III Corlux trial in about 440 patients who will receive a once-daily dose of either 300, 600 or 1200 mg of Corlux or placebo for 7 days. CORT has an SPA for this trial and the compound has Fast Track designation from FDA (see BioCentury, Sept. 6).

**Gilead Sciences Inc.** (GILD), Foster City, Calif.
Product: GS 7340
Business: Infectious
Molecular target: NA
Description: Prodrug of tenofovir
Indication: Treat HIV
Endpoint: Safety over 14 days of monotherapy and evaluate potency
Status: Phase II/III discontinued
Milestone: N/A
In a dose-escalation, double-blind Phase II/III trial in 30 patients, GILD said GS 7340 does not differentiate itself from the company’s other HIV products in clinical testing and on the market to an extent that supports further development.

Product: GS 9005
Business: Infectious
Molecular target: HIV protease

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**Aastrom Biosciences Inc.** (ASTM), Ann Arbor, Mich.
Product: Tissue Repair Cells (TRCs)
Business: Musculoskeletal
Molecular target: NA
Description: TRCs made from bone marrow, containing adult stem cells using AastromReplicell System
Indication: Treat maxillary jaw thinning requiring bone graft for dental implants
Endpoint: N/A
Status: N/A
Milestone: N/A
A STM began a Spanish trial in 5 patients to compare TRC treatment with a standard therapy.

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In an open-label Phase I/II trial in 16 patients, GS 9005 did not give a sufficient antiviral response. Based on these results, GILD discontinued development of GS 9005.

**Insmed Inc.** (INSM), Glen Allen, Va.
Product: INSM-18
Business: Cancer
Molecular target: Insulin-like growth factor-1 (IGF-1) receptor; HER-2/neu
Description: Insulin-like growth factor, small molecule tyrosine kinase inhibitor
Indication: Treat relapsed prostate cancer
Endpoint: Maximum tolerated dose; prostate specific antigen (PSA) levels
Status: Phase I start
Milestone: NA
INSM will begin this month a dose-escalating, U.S. Phase I trial in about 30 patients.

**MedImmune Inc.** (MEDI), Gaithersburg, Md.
Product: CAIV-T vaccine
Business: Infectious
Molecular target: NA
Description: Refrigerator-stable version of intranasal influenza vaccine
Indication: Prevent influenza virus
Endpoint: Safety, culture confirmed influenza
Status: Started Phase III
Milestone: Phase III data (mid-2005)
MED I began a double-blind, head-to-head, international Phase III trial in about 7,000 children aged 6-59 months comparing CAIV-T to injectable TIV vaccine.

Indication: Prevent influenza virus
Endpoint: Antibody response
Status: Completed Phase III enrollment
Milestone: Phase III data (mid-2005)
MED I completed enrollment of a double-blind, U.S. Phase III bridging study in 977 healthy volunteers comparing CAIV-T to MEDI’s FluMist.

**Polydex Pharmaceuticals Ltd.** (PO LX F), Toronto, Ontario
Product: Ushercell
Business: Infectious
Molecular target: NA
Description: Cellulose sulfate microbicidal gel
Indication: Prevent HIV and other sexually transmitted infections
Endpoint: Prevention of sexual transmission of HIV; prevention of sexual transmission of Neisseria gonorrhoeae and Chlamydia trachomatis
Status: Started Phase III

Milestone: Final Phase III data (2008)
PO LX F began a double-blind, placebo-controlled, Nigerian Phase III trial in 2,160 high-risk HIV negative women.

**Sunesis Pharmaceuticals Inc.**, Redwood City, Calif.
Product: SN S-595 (SPC -595)
Business: Cancer
Molecular target: NA
Description: Naphthyridine compound that induces cell cycle arrest and apoptosis
Indication: Treat advanced solid tumors
Endpoint: Safety; pharmacokinetics
Status: Started Phase I
Milestone: Start Phase II (2005)
Sunesis began an open-label, dose-escalation Phase I trial in 30-40 patients who will receive SN S-595 weekly on days 0, 7 and 14 followed by a 14-day observation period. The product also is in a single-dose Phase I trial for this indication.

**VaxGen Inc.** (VX GN ), Brisbane, Calif.
Product: LC16m8
Business: Infectious
Molecular target: NA
Description: Second generation, attenuated smallpox vaccine
Indication: Prevent smallpox
Endpoint: Assessment of neutralizing antibody, rates of adverse events
Status: Started Phase II/II
Milestone: NA
VX GN began a U.S. Phase I/II trial in about 150 healthy volunteers comparing LC16m8 with Dryvax smallpox vaccine. Dryvax is marketed by Wyeth (W YE, Madison, N. J.).

**OTHER RESEARCH NEWS**

**Millennium Pharmaceuticals Inc.** (MLNM), Cambridge, Mass.
Product: Personalized medicines
Use: Treat RA
MLNM’s studies using an RA patient registry containing genetic and proteomic data from about 1,000 patients identified biomarkers indicative of treatment success with disease modifying anti-rheumatic drugs (D MARDs). Specifically, they found elevated serum proteins, MMP3 and TNFR1, correlated with physician global assessment scores (PGA) and the number of painful and swollen joints. Also, MLNM found that 15 of 30 known risk genes for RA work in aggregate to account for estimated genetic risk of developing RA. The studies, which were conducted with Brigham and Women’s Hospital, will aid in the development of personalized medicines for RA, the company said. Data were presented at the American College of Rheumatology meeting in San Antonio.

**Vitra Bioscience Inc.**, Mountain View, Calif.
**Bristol-Myers Squibb Co.** (BMY), Princeton, N. J.
Product: CellICard
Use: Multiplexed cellular analysis
The partners announced that data obtained from multiplexed assays using CellICard system correlated with the results obtained from singleplex assays. The CellICard system allows up to 10 targets per cell line to be assayed in a single microtiter well. Data were presented at Assays and Cellular Targets meeting in San Diego.
OFTENINGS & SECURITIES TRANSACTIONS

Completed Offerings

Active Biotech AB (SSE:ACTIB), Lund, Sweden
Business: Cancer, Autoimmune
Date completed: 10/22/04
Type: Private placement of convertible debentures and warrants
Raised: SEK150 million ($20.6 million)
Underwriter: MGA Holding
Shares outstanding prior: 33.7 million
Note: ACTIB sold 3.8 million 4-year debentures that bear 2% annual interest and convert into ACTIB shares at SEK40, a 1% premium over ACTIB's Oct. 21 close of SEK39.50.

BioXell SpA, Milan, Italy
Business: Genitourinary, Endocrine, Autoimmune
Date completed: 10/20/04
Type: Venture financing
Raised: €23 million ($28.7 million)
Investors: BB Biotech; NIF Ventures; Qventures; MedImmune Ventures; Domain Associates; Prospect Venture Partners; MedImmune Ventures; Care Capital; Bio*One Capital

Business: Diagnostics, Microarrays, Proteomics
Date completed: 10/21/04
Type: Venture financing
Raised: $7.5 million
Investors: Oxford Biosciences Partners; Rock Maple Ventures; Fletcher Spaght Venture Partners; and other investors

GeneMedix plc (LSE:GMX), London, U.K.
Business: Generics
Date completed: 10/20/04
Type: Placing
Raised: £292,000 ($529,938)
Shares: 2.5 million
Price: 11.7p
Shares after offering: 315.5 million
Advisor: Southridge Capital Management
Note: Of the 2.5M shares issued, 2.4M shares were placed at 11.7p. These investors received warrants to purchase 1.8 million ordinary shares at 14.9p. The remaining 112,000 shares were placed at 12.5p.

Icoria Inc. (ICO R), Research Triangle Park, N.C.
Business: Functional genomics, Agbio/Environmental
Date completed: 10/21/04
Type: Private placement of convertible notes and warrants
Raised: $5 million
Shares outstanding prior: 36.2 million
Investor: Laurus Master Fund
Note: The notes mature in 2007, bear interest of prime plus 2.5% and convert into shares at $0.53, which is a 26% premium over ICO R's Oct. 20 close of $0.42. The investor also received warrants to purchase 1.7 million shares at $0.79.

Medical Discoveries Inc. (MLSC), Twin Falls, Idaho
Business: Infectious
Date completed: 10/20/04
Type: Private placement of convertible preferred stock and warrants
Raised: $1.2 million
Placement agent: Ascendiant Securities
Shares outstanding prior: 90.3 million
Investors: Mercator Advisory Group

Synairgen plc, Southampton, U.K.
Business: Cardiovascular
Date completed: 10/20/04
Type: IPO
Raised: £10 million ($18 million)
Shares: 7.7 million
Price: 130p
Shares after offering: 21.7 million
Advisor and broker: Robert W. Baird
Note: Synairgen expects to list on the London Stock Exchange's AIM on Oct. 26 with a post-money valuation of £28.8 million. Originally, the company expected a post-money valuation of £25 million. Existing shareholder Southampton Asset Management sold £500,000 ($900,000) in the IPO to satisfy demand for Synairgen's shares.

Vanda Pharmaceuticals Inc., Rockville, Md.
Business: Neurology
Date completed: 10/18/04
Type: Venture financing
Raised: $37 million
Investors: Domain Associates; Prospect Venture Partners; Rho Ventures; MedImmune Ventures; Care Capital; Bio*One Capital

ViroPharma Inc. (VPHM), Exton, Penn.
Business: Infectious
Date completed: 10/18/04
Type: Private placement of notes and warrants
Raised: $62.5 million
Shares outstanding prior: 26.2 million
Note: The senior notes bear 10% annual interest until Feb. 18, 2005, after which the rate will increase by 2% each month until the maturity date of Oct. 18, 2005. VPHM also issued warrants to purchase 5 million common shares. The company plans to exchange both the notes and warrants for $62.5 million of 6% senior convertible notes that are due in 2009 and have an initial conversion price of $2.50. VPHM closed Friday at $2.96.

Proposed Offerings

Zonagen Inc. (ZONA), The Woodlands, Texas
Business: Genitourinary, Cancer
Date announced: 10/20/04
Type: Follow-on
Shares: 4 million
Underwriter: Punk
Note: Zonagen raised €1.5M in an extension of its series A round, bringing to €5 million the total raised. Additional funding was led by Truffle Venture and included existing investor Europe Innovation.

Other Financial News

BioProgress plc (AIM:BPRG; BPRG), March, U.K.
Business: Drug delivery
Date announced: 10/21/04
The company listed its ADRs on NASDAQ under the symbol BPRG. Its shares will continue to trade on the London Stock Exchange's AIM under the same symbol. JPMorgan is the company's U.S. depositary for its ADRs.

Bioscience Managers Ltd., London, U.K.
Business: Other
Date announced: 10/21/04
Bioscience Managers closed the BML International Maple Leaf Fund I. The fund will invest in mid- to late-stage Canadian life science companies. BML said it expects to make 3-4 investments averaging C$5-C$10 million over the next 18-24 months. Teachers' Private Capital, the private equity arm of the Ontario Teachers' Pension Plan, will be the lone investor in the fund.

Celgene Corp. (CELG), Warren, N.J.
Business: Cancer, Inflammation
Date announced: 10/21/04
CELG's board approved a 2-for-1 split of the company's 82 million shares outstanding. The company will begin trading on a post-split basis on Oct. 25.

Neovacs SA, Paris, France
Business: Infectious, Cancer
Date announced: 10/18/04
Neovacs raised €1.5M in an extension of its series A round, bringing to €5 million the total raised. Additional funding was led by Truffle Venture and included existing investor Europe Innovation.

‘It’s the BioCentury’™