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BioCentury

THE BERNSTEIN REPORT ON BIOBUSINESS™

2012 Financial Markets Preview

Living creatively

By Stacy Lawrence
Senior Writer

For small, early stage biotech companies, 2012 could be the year of living creatively.

Although public biotechs raised more funds last year than ever before, the vast majority of the money was debt financing by established companies with marketed products. Thus while the overall numbers look good and are likely to continue to do so, precommercial companies will have to get creative with their financings.

Many of these companies avoided raising money in 2011 because they didn't like the valuations, but Wall Streeters say they are now running out of cash. As a result, they will have to use the tricks at hand — underwritten offerings via an empty S-1 filing, at-the-market offerings, and going public via Form 10 — to raise money at whatever valuations they can get.

At the same time, investors who sat on their hands in 2H11 to protect their returns may feel freer to pick up bargains early in the year since they won't be judged on their performance again until late in 2012.

Companies that can't tap the public markets — or have given up — will be hoping for another year of robust M&A, as the deals that closed in 2011 reached an all-time high both in number and transaction value.

Setting the stage

Development stage biotechs are getting a shrinking share of an expanding pie. And in absolute terms, their money raised has remained static. The trend is likely to continue as long as the sector remains out of favor among generalist investors and debt is a cheap and viable alternative for large and mid-cap companies *(see "The 1% Effect," page 2)*.

> ***"As the capital markets continue to be difficult, traditional investors are able to extract terms that are more and more onerous."***
>
> **Todd Wyche, Brinson Patrick**

In 2011, public biotechs raised $43 billion, easily eclipsing the record $33.1 billion in 2000. But debt accounted for 82% of the total dollars raised, compared to only 19% in 2000 *(see "Debt Dominance," page 3)*.

Excluding debt, 2011 was lackluster at best. Development stage companies without products in registration or on the market received only 10% of the total funds raised, down from 13% in 2010. In dollar terms, the number was up slightly from $4.1 billion to $4.4 billion *(see "Funding by Stage," page 4)*.

During the last biotech financing boom in 2007, development stage companies accounted for more than one-third of the sector's public financing activity.

Last year, Phase II companies raised $1.8 billion, which was only 4% of total public biotech fundraising. Indeed, the amount raised by public Phase II companies actually was down from $1.9 billion in 2010.

Private Phase II companies raised $1.4 billion. Indeed, VCs played a role in both types of offerings and are increasingly being called upon to foot the bill for both public and private Phase II players.

"It's a very tough environment, one of the tougher situations for early stage money raising in my 25-year experience," noted Viren Mehta of Mehta Partners. "Many companies don't have any option but to raise at lower valuations."

He added: "Many companies are not able to defer any longer. The moment comes for many companies when they have to swallow hard and accept painful dilution."

Cash on hand

Market volatility and macroeconomic risk had most buysiders sitting on the sidelines through the back half of 2011. Bankers are hopeful that this year will be more stable, in which case investors might be willing to support more deal flow during 1H12 *(see "Fear Factor," page 5)*.

"Cash on the sidelines is at record levels in generalist and fundamental funds," said John Chambers of Roth Capital Partners. He noted that several investors cashed out with M&A transactions last year including the $11 billion that **Gilead Sciences Inc.** paid for **Pharmasset Inc.**; the $20.1 billion acquisition of **Genzyme Corp.** by **Sanofi**; and the $6.8 billion that **Teva Pharmaceutical Industries Ltd.** paid for **Cephalon Inc.**

"I think we'll see a great deal of transactional activity and funds looking to deploy capital; they have several quarters until they are evaluated again," said Chambers. "If companies perform and deals trade up, we could see the market open up pretty significantly."

Matthias Spaenle of Oppenheimer sees potential for the buyside to become more risk tolerant in the new year. "It will be a function of a better macroeconomic environment and people starting to make money in real home runs like Pharmasset and Inhibitex," he said.

Pharmasset shares climbed 489% last

See next page

2012 Financial Markets Preview,
from previous page

year to finish at $128.20. Fellow HCV play **Inhibitex Inc.** was up 321% to $10.94 on positive Phase Ib data and investor expectations that it, too, might be acquired.

Given the cash sitting in the 75 or so active biotech funds, Michael Brinkman of Jefferies said he expects a busy calendar in the first quarter, as a number of his clients are planning significant transactions.

"For companies that are in Phase III or later, there's tremendous access to capital. For companies that are earlier stage, it's much more challenging," he said.

Among development stage companies, buysiders are looking for at least two years of cash and strong proof of concept data, along with an undeniable market need.

"The pool of investors who are willing to write a check before they see randomized data is very small, and they will demand punitive valuations to compensate for risk," said RBC's Andrew Singer.

For these companies, financing prospects remain grim.

"We met with a company that has a Phase III program to fund — they need $50 million to fund two Phase III trials, and their market cap is less than $50 million," said Josh Muntner of ThinkEquity. "It's hard to see how they'll pay for the trials."

Muntner said the company is caught in a Catch-22: investors don't want to buy stock until the company has money in the bank, but the company can't get money until investors will buy the stock.

Victim of success

Adding to the financing challenge is the fact there are more options than ever for biotech buysiders. The ranks of companies over $1 billion have grown, as have those with marketed products and actual revenue.

"I can remember in 1998 when there were only a dozen biotech companies with market caps north of $1 billion," said David Strupp of Rodman & Renshaw. "If you were a biotechnology investor 15 years ago, you needed to invest in smaller cap, development stage companies in order to maintain a diversified portfolio. Now there's such a wealth of opportunity in de-risked, larger-cap companies that either have revenues or a much later-stage development pipeline."

Generalist funds are typically looking only at the 61 companies with market caps of $1 billion of more.

"Today, some of the larger biotechnology funds are managing billions of dollars of assets," Strupp noted. "A fund of that size can't move the needle investing in a $50 million market cap company. Many investors are willing to miss the potential for significant upside and would prefer to buy into a de-risked story at loftier valuations."

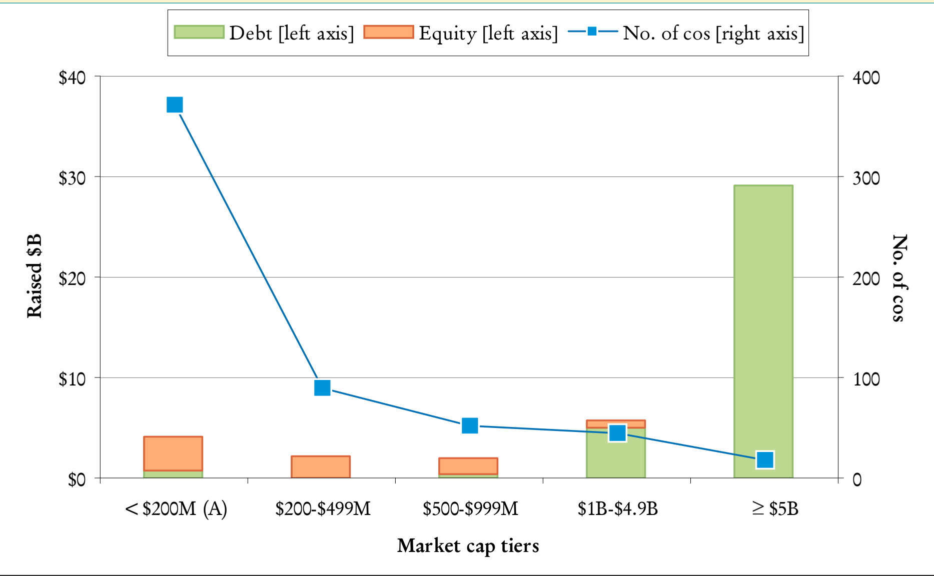
Stuart Duty of Piper Jaffray agreed. He noted that even sector specialists "can invest an entire portfolio and not have a development stage company in it."

See next page

The 1% effect

Nine public biotechs valued above $5 billion — representing less than 2% of the more than 570 companies tracked by BioCentury — pulled in more than two-thirds ($29.1 billion) of the record $43 billion raised in the public markets in 2011. All the money raised by the nine came from debt deals.

The nine companies were **Amgen Inc.** (NASDAQ:AMGN); **Gilead Sciences Inc.** (NASDAQ:GILD); **Illumina Inc.** (NASDAQ:ILMN); **Laboratory Corp. of America Holdings** (NYSE:LH), which acquired Orchid Cellmark Inc. last year; **Quest Diagnostics Inc.** (NYSE:DGX), which acquired Celera Corp. last year; **Teva Pharmaceutical Industries Ltd.** (NASDAQ:TEVA); **UCB Group** (Euronext:UCB); **Valeant Pharmaceuticals International Inc.** (TSX:VRX; NYSE:VRX); and **Warner Chilcott plc** (NASDAQ:WCRX). The analysis based on market caps at the end of 2010. (A) More than 370 companies, including thinly traded securities on OTC Bulletin Board and Pink Sheets; *Source: BCIQ: BioCentury Online Intelligence*



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2012 Financial Markets Preview,
from previous page

A case in point is venBio. "We look at our portfolio and it's more commercial-oriented than ever before. Close to half the portfolio is in micro-cap companies that are revenue-generating," the firm's Kurt von Emster said.

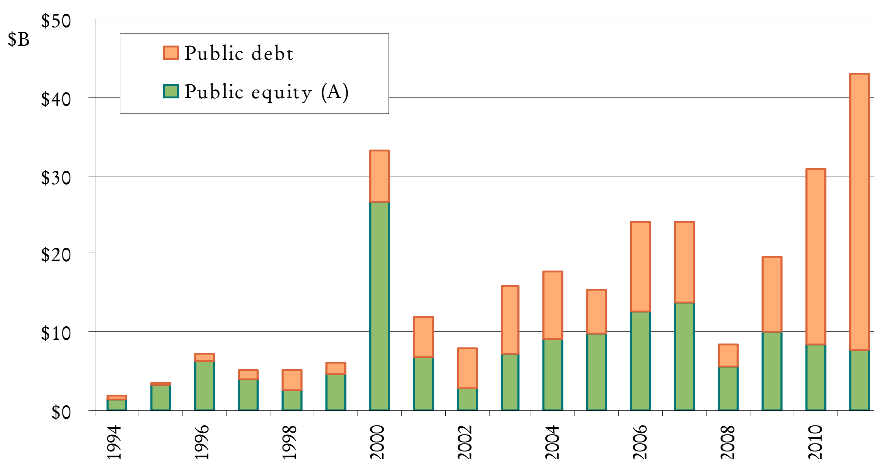
He cited as examples neurology and gastrointestinal company Adolor Corp.; drug delivery company **Depomed Inc.**; GI company **Santarus Inc.**; and pulmonary and infectious disease company **InterMune Inc.**

Adolor was acquired by **Cubist Pharmaceuticals Inc.** for $221 million in December.

Debt dominance

The amount of debt raised by public biotechs has been rising. Last year, debt accounted for $35.3 billion (82%) of the $43 billion total raised in the public markets. Seven public companies alone completed $1 billion-plus debt deals, raising $27.5 billion. In 2010, debt accounted for $22.4 billion (73%) of the $30.7 billion total raised in the public markets, with eight companies raising $16.8 billion in $1 billion-plus deals.

Prior to 2010, money raised from debt as a percentage of the total raised in the public markets ranged from as low as 5% in 1995 to as high as 67% in 2002. (A) IPOs, follow-ons, PIPEs and other equity deals; *Source: BCIQ: BioCentury Online Intelligence*



Volatility adjusted

By necessity, publicly held development stage biotechs have become increasingly sophisticated at accessing capital.

Of the $4.4 billion raised by these companies in 2011, about 22% came from standard offerings such as PIPEs and registered directs. There were 85 PIPE deals that raised a total of $680 million and 19 registered directs that brought in a total of $282 million.

The average amount raised in these types of offerings has been steadily shrinking since the salad days of 2007. Life sciences PIPEs raised an average of $8 million last year, down from $18.4 million in 2007. Registered directs raised an average of $14.9 million last year, down from $27.7 million in 2007.

"PIPEs are getting smaller and smaller. I see these $1.5 million PIPE transactions. Some of them finance a company for about a month; I'm not sure what's the point," said Matt Geller of Geller Biopharm.

"Only issuers who have no other choice are doing PIPEs," said Annette Grimaldi of BMO.

Investors typically don't want PIPEs because the shares are unregistered, while other funding vehicles give them registered shares that can be sold immediately.

"PIPEs are becoming increasingly difficult to execute as investors have expressed a preference for receiving registered securities — either offered off of a shelf registration or Form S-1," said Strupp.

Strupp and Chambers noted there is an emerging alternative that allows non-shelf eligible biotechs — those that don't meet the requirements for filing a Form S-3 with the SEC — to sell registered shares. The process involves filing a Form S-1 that doesn't include details and then filing a detailed S-1 just prior to the offering of registered shares.

"We advise our clients to be prepared. If they are S-3 eligible, certainly keep it up and in shape. For those companies that aren't S-3 eligible and don't have a shelf, we file an S-1 initially without managers on it, then we put the managers on it and sell registered shares," said Chambers. "This is the best vehicle in this market. It provides you the size of financing with less onerous terms and lacks the encumbrances of debt."

Stealth mode

Confidentially marketed public offerings, a type of follow-on that is marketed privately and then flipped public at the last minute, are likely to continue gaining traction. These vehicles seek to dampen volatility by shrinking the window of time in which a stock can decline following announcement of an offering.

> ***"In 2012, we will see more companies acquired than IPO. That will be a nice metric to see. We've been overburdened with supply for the last 20 years."***
>
> **Kurt von Emster, venBio**

"Public companies understand and recognize the volatility out there," said Peter Reikes of Stifel Nicolaus Weisel. "Companies are trying to do confidential processes and are avoiding public deals wherever they can because that's where the market can really extract its pound of flesh. North of three-quarters of the public company equity issuances are done on a confidential basis."

According to Duty, companies that opt for a fully marketed follow-on risk a share price discount that is "generally 20% greater than privately marketed offerings that are flipped public. We expect most companies to pursue the private route."

At $2.6 billion, follow-ons accounted for more than half of the funds raised by development stage biotechs last year. But the average size of these deals — including confidentially marketed and plain vanilla follow-ons — also shrank to $50.1 million last year from $71.8 million in 2007 *(see "Follow-On Performance," page 6)*.

ATM machines

While confidentially marketed financings seek to minimize volatility, at-the-market

See next page

2012 Financial Markets Preview, *from previous page*

offerings seek to exploit it.

In ATMs, companies sell shelf-registered shares over time directly into the market — usually a small amount of stock over the space of a few days.

In 2009, there were only about 10 biotech ATMs filed worth up to $250 million. The following year, there were about 20 worth up to $425 million.

In 2011, the number of biotech ATMs grew to more than 30 worth around $600 million, according to Robert Dentice of Cantor Fitzgerald. He expects to see about 50 ATMs put in place this year.

Companies generally pay a 3-5% fee for ATMs.

By comparison, Todd Wyche of Brinson Patrick noted that including the underwriter fee, discounts and warrants, the total cost of capital in traditional deals such as PIPEs, registered directs and follow-ons climbed to an average of 26% in the third quarter from 20% in the second quarter.

"As the capital markets continue to be difficult, traditional investors are able to extract terms that are more and more onerous," he said.

Wyche cited as an example the right of first refusal, in which a company agrees as part of a traditional financing to return to the same investor for a subsequent financing or that it will not do a transaction in the future at better terms.

ATMs do have limitations, since only a relatively small amount of capital can be raised at one time and companies need a decent amount of liquidity. Another criticism of ATMs is that bankers typically have no control over who is acquiring the shares.

Nevertheless, Cantor anticipates about $1 billion worth of life sciences ATMs will be done annually. Indeed, Dentice predicted that about half of the shelf-eligible life sciences companies will eventually put an ATM in place.

One high profile example is Inhibitex, which established an ATM program in 2010 through McNicoll, Lewis & Vlak. In November 2011, the company capitalized on its good year by raising $20 million through the program.

"They had a great situation, where they raised $20 million in a couple of days at a very good share price," said Dean Colucci of MLV. Inhibitex sold shares at $10.25 near the end of November, having started the month at around $4.

"In a volatile market, where you have 400- to 500-point index moves in a day, we've been able to raise $1-$3 million over a couple of days for a $100-$150 million market cap company. If that's done over several months it can add up to $5-$10 million. Given the macro conditions, there's an increasing acknowledgement that the ATM product works," Colucci added.

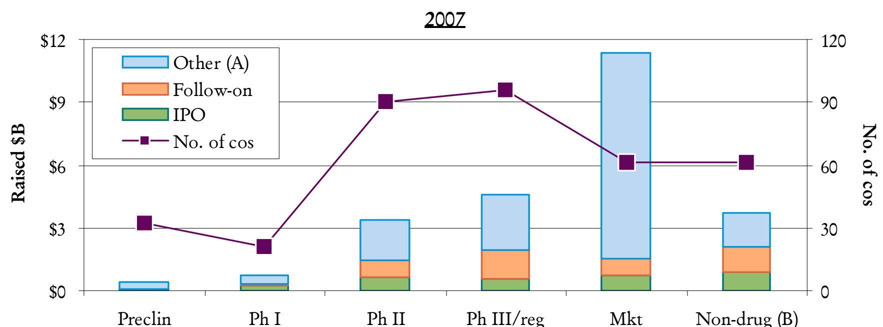
Muntner said ThinkEquity has started to offer an ATM program that puts shares into the hands of fundamental, long-only buyers.

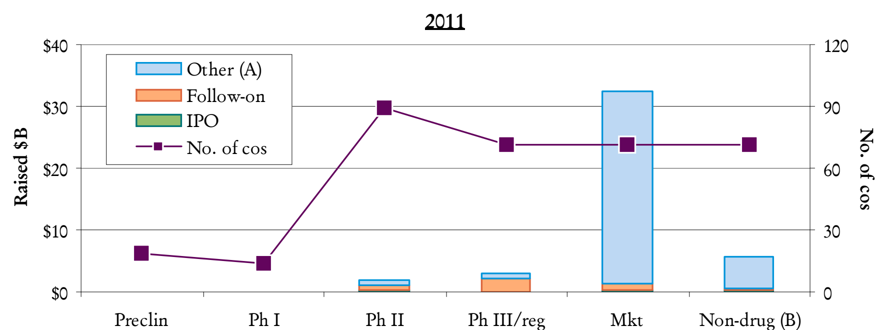
"We have had conversations on the ATM product with companies over a billion dollar market cap. They could do any sort of financing and are including this as an option," he said.

Funding by stage

While public biotechs raised a record-breaking $43 billion in 2011, more than 75% of the money went to 71 companies with marketed drugs. Debt deals by five companies with marketed drugs — **Amgen Inc.** (NASDAQ:AMGN), **Gilead Sciences Inc.** (NASDAQ:GILD), **Teva Pharmaceutical Industries Ltd.** (NASDAQ:TEVA), **Valeant** (NYSE:VRX; TSX:VRX) and **Warner Chilcott plc** (NASDAQ:WCRX) — accounted for $24.7 billion, or 57%, of the annual total.

In 2007, prior to the economic crisis, public biotechs raised $24.1 billion. Only 47% of the total went to 61 companies with marketed drugs. And 53 companies with lead programs in preclinical or Phase I testing raised $1.1 billion in 2007 vs. 33 that raised a paltry $179 million in 2011. The figures below are based on the stage of development at the time of each financing. (A) Includes PIPEs, registered directs, other equity deals and debt; (B) Includes diagnostic, supply/service and device companies; *Source: BCIQ: BioCentury Online Intelligence*





Other than IPO

Bankers and buysiders are looking forward to a couple of high-profile IPOs going into 2012, but no one expects the market for new issues to gain any real momentum. Most are looking for alternatives.

Cancer company **Merrimack Pharmaceuticals Inc.**, which filed in July to raise up to $172.5 million, has the largest proposed offering in the 12-company IPO queue.

Other IPO filings are expected to come this year from the likes of cancer and Orphan disease company **Acceleron Pharma Inc.** and cardiovascular, autoimmune and cancer company **Portola Pharmaceuticals Inc.** *(see "IPO Queue," page 7)*.

The alternative routes to the public markets include the Form 10 pathway and Regulation A reform.

A handful of companies with crossover investors are successfully using Form 10. They are raising money, becoming

See next page

2012 Financial Markets Preview,
from previous page

publicly reported, trading on the OTCBB and then listing on a major exchange. The process occurs within the span of a few months.

In addition, the reverse merger is losing its stigma as a sign of weakness.

Marina Bozilenko of William Blair cited **Synageva BioPharma Corp.** as a "reverse merger out of strength, not desperation." In November, the rare disease company completed a reverse merger with Trimeris Inc.

"Synageva did a very clever deal. They could have gone public on their own; they had a bunch of cash. Trimeris also brought in a bunch of cash," she said.

At Sept. 30, Trimeris had $52.4 million in cash. Synageva filed a $100 million shelf registration in December.

There also are proposals before Congress that would make it easier for private companies to access the public markets, including an update to Reg A.

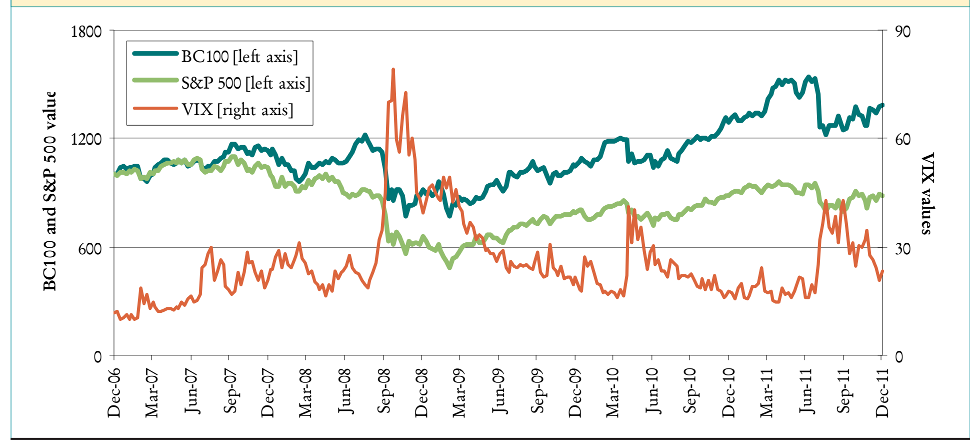
In November, the House passed the Small Company Capital Formation Act (H.R. 1070), which would allow companies to raise up to $50 million in public offerings over 12 months without being subject to the stricter registration and paperwork SEC currently requires for offerings of more than $5 million. The Senate version (S.1544) was introduced in September and has been sent to the Committee on Banking, Housing, and Urban Affairs.

Fear factor

The Chicago Board Options Exchange Market Volatility Index (VIX) is a measure of the expected volatility in the S&P 500 over the next 30 days. It fell below the 30 mark at the end of last year, indicating the potential for an end to the bearish sentiment that has plagued the markets for most of the last five months. Generally, market watchers consider investor sentiment to be overly bearish when the VIX is above 30.

The last time the index was above 30 for an extended period was in May 2010, when a trading algorithm along with the debt crisis in Greece sparked a sharp downturn in the markets. The BioCentury 100 is up 28% since the VIX fell below 30 in June 2010, while the broader market, as gauged by the S&P 500, is up 15%.

Similarly, the VIX traded above 30 for about eight months during the 2008-09 economic crisis. The BC100 and S&P 500 are up 53% and 37%, respectively, since the VIX went below 30 in June 2009. BC100 and S&P 500 indexed to 1,000 as of Dec. 29, 2006.



Darwin and VCs

Buysiders and bankers are paying more attention than ever before to life sciences VCs, in large part because they have been supporting young public companies.

For example, Mike Powell of Sofinnova Ventures, which closed a $440 million fund in October 2011, said up to 25% percent of the new fund may be allocated for public company investment. The prior fund's allocation was about 20%.

But not all VCs are in a position to do that.

"One of the things that is a bit concerning is that healthcare VCs are really, really pulling back," said Sven Borho of OrbiMed Advisors. "A lot of them, especially early stage guys, can't raise new funds. There are fewer strong players."

According to von Emster, as the pressure has mounted, VCs have invested as much money into IPOs and secondary offerings for public companies as they have into private companies. "We're at a tail end of an investment cycle for a lot of these funds. This is their last gasp to get companies to an exit," he said.

At the same time, some buysiders think a thinning of the ranks among VCs and the companies they support will be good for the sector.

"The VCs have been forced into a Darwinian phase. There will be dramatically fewer biotechs created in the coming years — we've already seen that drop. There has been an equilibrium of new company creation," von Emster said. "In 2012, we will see more companies acquired than IPO. That will be a nice metric to see. We've been overburdened with supply for the last 20 years."

> ***"You may have a willing buyer and a willing seller, but they can't agree on the price as prices fluctuate. That might be one of the gating factors of corporate transactions."***
>
> **Les Funtleyder, Miller Tabak**

Andrew Bogan of Bogan Associates agreed. "VCs did themselves no favors by massively over-raising capital" for early stage companies, he said. "They've got a decade now of too much capital chasing too few opportunities."

Bogan expects public investing by life sciences VCs to accelerate in the coming years as they chase returns.

"They can't start businesses unless they have the performance. We need to see LPs shift capital into equities and then see returns there. Then we will see VCs recover," he said.

Acquisitive stage

A record number of private companies disappeared in the mergers and acquisitions that were completed in 2011, and the dollar volume of both private and public takeouts that closed also reached new heights *(see "M&A Activity," page 8)*.

Always hopeful for more M&A, bankers and buysiders expect the pressure on VCs could result in more takeouts, particularly for later stage assets, companies with marketed products and winners in HCV.

See next page

Follow-on performance

Follow-on deals slowed in the second half of 2011, with only 25 deals completed for $1.2 billion vs. 54 deals for $3 billion in 1H11. For the year, follow-ons raised a total of $4.2 billion, more than the $3.5 billion raised in 2010, but still below the $6.2 billion raised in 2009. The follow-on group is down a median of 6%, but a few companies — notably in the HCV space — posted significant gains after raising money.

The market value for **Idenix Pharmaceuticals Inc.** (NASDAQ:IDIX) is up 201% and 15%, respectively, since completing follow-ons in April and November. **Inhibitex Inc.** (NASDAQ:INHX) is up 167% since its $47 million follow-on in April, and **Pharmasset Inc.** (NASDAQ:VRUS), which is being acquired by **Gilead Sciences Inc.** (NASDAQ:GILD) for $11 billion, is up 177% since its $129.5 million follow-on in January. (A) Median percent change calculated for quarterly and full-year periods; (B) Follow-ons of units consisting of stock and warrants are excluded from the post-money and percentage change calculations because the price per share was not available; $M; *Source: BCIQ: BioCentury Online Intelligence*

Company	Date	Raised	Post-$	12/30 mcap	% chg (A)
Orexigen Therapeutics Inc. (NASDAQ:OREX) (B)	12/22/11	$90.0	NA	$86.5	NA
StemCells Inc. (NASDAQ:STEM) (B)	12/16/11	$10.0	NA	$18.4	NA
Ariad Pharmaceuticals Inc. (NASDAQ:ARIA)	12/15/11	$257.6	$1,641.6	$1,929.9	18%
Synergy Pharmaceuticals Inc. (NASDAQ:SGYPD) (B)	12/13/11	$17.3	NA	$189.4	NA
Novelos Therapeutics Inc. (OTCBB:NVLT)	12/7/11	$6.0	$22.0	$16.2	-26%
Inovio Pharmaceuticals Inc. (NYSE-A:INO)	12/7/11	$4.0	$69.6	$57.8	-17%
Exact Sciences Corp. (NASDAQ:EXAS)	12/6/11	$28.8	$452.0	$458.8	1%
Cadence Pharmaceuticals Inc. (NASDAQ:CADX)	11/22/11	$81.8	$320.3	$337.4	5%
Pacira Pharmaceuticals Inc. (NASDAQ:PCRX)	11/16/11	$52.3	$164.3	$218.7	33%
Idenix Pharmaceuticals Inc. (NASDAQ:IDIX)	11/16/11	$61.1	$686.1	$786.3	15%
Adventrx Pharmaceuticals Inc. (NYSE-A:ANX) (B)	11/16/11	$17.0	NA	$28.2	NA
Dynavax Technologies Corp. (NASDAQ:DVAX)	11/3/11	$69.0	$383.0	$508.7	33%
Catalyst Pharmaceutical Partners Inc. (NASDAQ:CPRX)	11/2/11	$3.5	$28.2	$31.9	13%
4Q follow-ons (13 deals)		$698.3	$3,767.1	$4,668.0	13%
3Q follow-ons (12 deals)		$467.4	$3,142.2	$1,915.7	-40%
2Q follow-ons (25 deals)		$1,303.2	$7,559.9	$7,279.3	-10%
1Q follow-ons (29 deals)		$1,696.5	$12,792.1	$14,800.1	-5%
2011 total (79 deals)		$4,165.4	$27,261.2	$28,663.1	-6%

2012 Financial Markets Preview,
from previous page

"The real issue is just capacity," said Singer. "Pharmas are only able to do a certain number. They do an acquisition or two and then pause to integrate."

Another trend point is toward late stage deals, he added. "Pharmas are happy to pay more for something that is de-risked in Phase II and later. We won't see a lot of acquisitions of early Phase II assets."

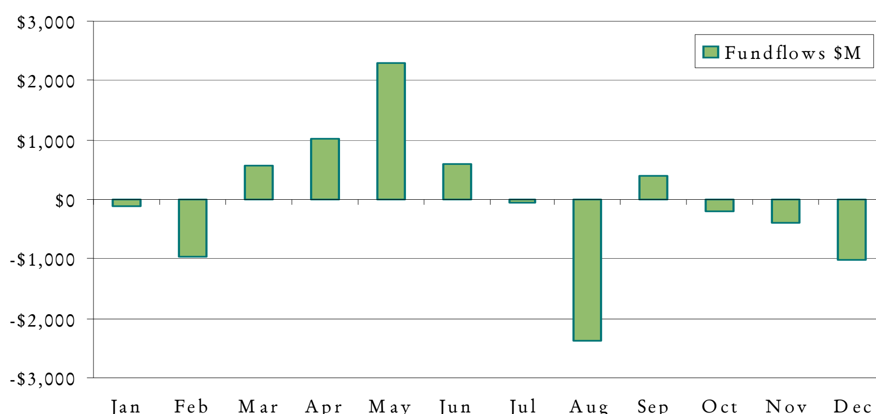
Strupp agreed. "Private companies that are fully financed through their Phase III data are terrific targets as they start to report in their pivotal data."

On the other hand, Grimaldi warned the market in 2012 will remain volatile, which could make M&A challenging. "You might think that M&A is countercyclical, but it's really not. Having said that, the fundamentals are still good for M&A. Large pharmas need to augment their pipelines,

See next page

Healthcare/biotech fund flows

About $231 million exited healthcare/biotech funds in 2011. In August, $2.4 billion flowed out of these funds as the U.S. debt debate along with negative news on sales of Provenge sipuleucel-T from **Dendreon Corp.** (NASDAQ:DNDN) led to a selloff in the sector and overall markets. The European debt crisis dominated the headlines in December, with $1 billion exiting the funds. Data below as of Dec. 21, 2011. *Source: EPFR Global*



2012 Financial Markets Preview,
from previous page

and VCs need to access the capital market," she said.

Les Funtleyder of Miller Tabak also noted that volatility inhibits M&A. "You may have a willing buyer and a willing seller, but they can't agree on the price as prices fluctuate. That might be one of the gating factors of corporate transactions," he said.

Several buysiders do expect deals in HCV.

von Emster sees HCV companies and beaten-up launch plays as potential acquisition targets. "HCV still has a number of unencumbered assets for sale; at least one of those will go," he said.

He noted that trading in 2011 was "long HCV and short drug launches. The first half of that still works, but the second half doesn't work. Investors have unduly penalized these drug launch companies."

Beaten down companies that launched drugs in the last few years include **Dendreon Corp.**, which is off 86% since launching prostate cancer immunotherapy Provenge sipuleucel-T; **Vertex Pharmaceuticals Inc.**, which is off 41% since launching Incivek telaprevir to treat HV; InterMune, which is off 72% since launching Esbriet pirfenidone to treat idiopathic pulmonary fibrosis (IPF); and **Human Genome Sciences Inc.**, which is off 75% since launching Benlysta belimumab to treat lupus.

"M&A activity among launch companies is starting to gain traction. But the majority will probably not be friendly. You don't want to sell a company when it's down," von Emster added.

More generally, Oppenheimer's Spaenle expects to see "a very active environment. We'll see a number of several billion dollar deals and see a few of the larger biotechs possibly disappear. We'll also see a lot of private companies being bought, which is a function of the perspective of the VCs."

Spaenle expects these will almost always be structured deals. "They get a little up front, but the back end often doesn't materialize," he noted.

Jefferies' Brinkman thinks M&A among companies valued over $1 billion could be

See next page

IPO queue

Five biotechs proposed IPOs in 4Q11, bringing the total in the queue to at least 12. Unless noted, the company is seeking to list on NASDAQ. (A) Status at time of filing; (B) Taiwan Liposomes Co. Ltd. has listed a small percentage of its shares on Taiwan's Emerging Market Board, an intermediate step in anticipation of an IPO on the Taiwan Stock Exchange; *Source: BCIQ: BioCentury Online Intelligence*

Company	Date filed	To be raised	Status (A)
Rib-X Pharmaceuticals Inc.	11/25/11	Up to $80M	Ph II
Tvax Biomedical Inc.	11/7/11	Up to $40M	Ph II
Verastem Inc.	11/3/11	Up to $50M	Preclin
ChemoCentryx Inc.	10/14/11	Up to $69M	Ph III
Cempra Pharmaceuticals Inc.	10/12/11	Up to $86.3M	Ph II
Argos Therapeutics Inc.	7/29/11	Up to $86.3M	Ph II
Merrimack Pharmaceuticals Inc.	7/8/11	Up to $172.5M	Ph II
LipoScience Inc.	6/23/11	Up to $86.3M	Mkt (diagnostic)
Intas Pharmaceuticals Ltd. (NSE; BSE)	3/25/11	Up to $94.8M	Mkt (drug)
Supernus Pharmaceuticals Inc.	12/23/10	Up to $100M	Registration
Taiwan Liposomes Co. Ltd. (Taiwan) (B)	9/27/10	TBD	Mkt (drug)
IASO Pharma Inc. (NYSE-A)	4/15/10	Up to $25M	Ph II

IPO performance

Nineteen biotechs raised $972.7 million via IPOs in 2011, including five companies last quarter. This compares to 31 IPOs that raised $1.6 billion in 2010. The 2011 class traded down a median of 19%, with 13 of 19 companies ending the year below their post-money valuation. The market values for traditional Chinese medicines company **Tibet Pharmaceuticals Inc.** (NASDAQ:TBET), small molecule discovery company **RaQualia Pharma Inc.** (JASDAQ:4579) and drug delivery company **AcelRx Pharmaceuticals Inc.** (NASDAQ:ACRX) all fell more than 60%.

Tibet's shares declined 22% the week in May it announced that the rising cost of raw materials had decreased its gross margin. Though RaQualia had almost no newsflow since its July IPO, it was down about 75% prior to the last week of the year, when it rallied after announcing a COX-2 licensing deal with the **Chinese Academy of Sciences** and **Guangzhou Great Water Tech Co. Ltd.** The stock ended the year down 61% from its IPO price. AcelRx announced in November that it would not advance its two lead compounds into Phase III testing without additional funding or a development partner. (A) Median percent change calculated for quarterly and full-year periods; $M; *Source: BCIQ: BioCentury Online Intelligence*

Company	Date	Raised	Post-$	12/13 mcap	% chg (A)
Chiome Biosciences Inc. (Tokyo:4583)	12/9/11	$6.5	$70.7	$67.8	-4%
Clovis Oncology Inc. (NASDAQ:CLVS)	11/15/11	$139.1	$290.7	$315.1	8%
NewLink Genetics Corp. (NASDAQ:NLNK)	11/11/11	$43.4	$131.1	$131.8	1%
3-D Matrix Ltd. (JASDAQ:7777)	10/14/11	$19.1	$122.6	$134.5	10%
SymBio Pharmaceuticals Ltd. (JASDAQ:4582)	10/11/11	$36.8	$138.2	$117.1	-15%
4Q IPO total (5 cos)		$245.0	$753.3	$766.3	1%
3Q IPO total (3 cos)		$213.6	$758.2	$455.5	-47%
2Q IPO total (4 cos)		$188.9	$646.6	$755.7	-6%
1Q IPO total (7 cos)		$325.2	$928.1	$696.4	-34%
2011 total (19 cos)		$972.7	$3,086.2	$2,673.8	-19%

2012 Financial Markets Preview,
from previous page

a driver for generalists.

"There are a number of new places to put your capital if you're looking for $1 billion-plus companies. The more we have, the more room there is for generalists to get involved. If there is continued success and acquisition of these companies, that could be the single biggest driver to get more participation from generalists," he said.

One banker cited **Algeta ASA**, **Medivation Inc.** and **Onyx Pharmaceuticals Inc.** as examples of companies in this group that might be ripe for takeout.

Algeta gained 13% last year on positive Phase III data for its Alpharadin to treat castration-resistant prostate cancer (CRPC) in June. Medivation was up 204% last year on positive Phase III data for MDV3100 to treat CRPC. Onyx was driven up last quarter on acquisition rumors and finished the year with a gain of 19%.

COMPANIES AND INSTITUTIONS MENTIONED

Acceleron Pharma Inc., Cambridge, Mass.
Algeta ASA (OSE:ALGETA), Oslo, Norway
Cephalon Inc., Frazer, Pa.
Cubist Pharmaceuticals Inc. (NASDAQ:CBST), Lexington, Mass.
Dendreon Corp. (NASDAQ:DNDN), Seattle, Wash.
Depomed Inc. (NASDAQ:DEPO), Menlo Park, Calif.
Genzyme Corp., Cambridge, Mass.
Gilead Sciences Inc. (NASDAQ:GILD), Foster City, Calif.
Human Genome Sciences Inc. (NASDAQ:HGSI), Rockville, Md.
Inhibitex Inc. (NASDAQ:INHX), Alpharetta, Ga.
InterMune Inc. (NASDAQ:ITMN), Brisbane, Calif.
Medivation Inc. (NASDAQ:MDVN), San Francisco, Calif.
Merrimack Pharmaceuticals Inc., Cambridge, Mass.
Pharmasset Inc. (NASDAQ:VRUS), Princeton, N.J.
Portola Pharmaceuticals Inc., South San Francisco, Calif.
Onyx Pharmaceuticals Inc. (NASDAQ:ONXX), South San Francisco, Calif.
Sanofi (Euronext:SAN; NYSE:SNY), Paris, France
Santarus Inc. (NASDAQ:SNTS), San Diego, Calif.
Synageva BioPharma Corp., Lexington, Mass.
Teva Pharmaceutical Industries Ltd. (NASDAQ:TEVA), Petah Tikva, Israel
Vertex Pharmaceuticals Inc. (NASDAQ:VRTX), Cambridge, Mass.

M&A activity

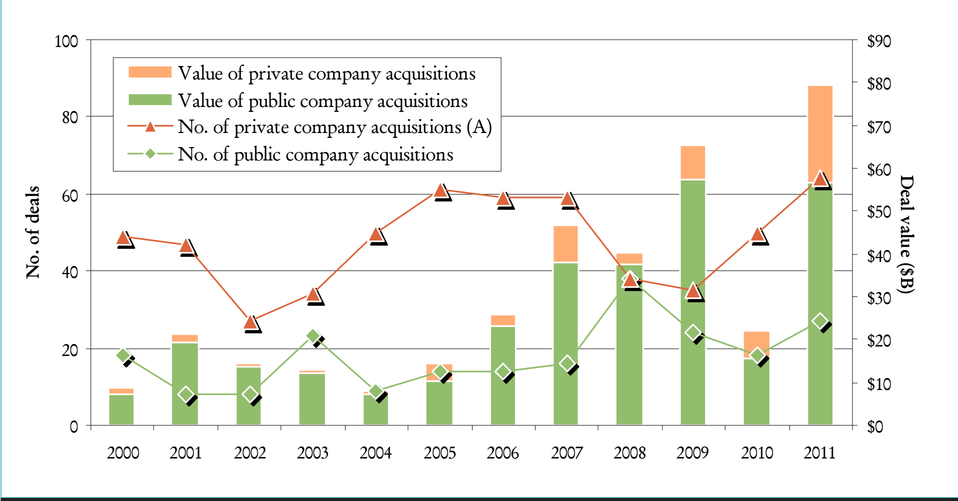
The total value of completed M&A transactions in 2011 reached a record $79 billion, largely driven by the takeouts of Genzyme Corp. and Nycomed. The 91 total deals, including private deals where financial terms were not disclosed, far exceeded the next biggest year, 2008, when 76 deals completed.

A record-breaking 64 private companies were acquired last year. Forty-six of those, where financial terms were disclosed, were purchased for an aggregate of $23 billion. The bulk of that total came from the $13.4 billion acquisition of Nycomed by **Takeda Pharmaceutical Co. Ltd.** (Tokyo:4502).

Along with Nycomed, at least six other privately held pharmaceuticals were acquired with the expressed goal of expanding into emerging markets: Bergamo by **Amgen Inc.** (NASDAQ:AMGN); Corporacion Infarmasa S.A. by **Teva Pharmaceutical Industries Ltd.** (NASDAQ:TEVA); Dr. F. Frik Ilac A.S. by **Recordati S.p.A.** (Milan:REC); Laboratorios Farmacol S.A. by Nycomed, prior to its being acquired by Takeda; NovaMed Pharmaceuticals Inc. by **SciClone Pharmaceuticals Inc.** (NASDAQ:SCLN); and PharmaSwiss S.A. by **Valeant Pharmaceuticals International Inc.** (NYSE:VRX; TSX:VRX). The 2011 tally does not include the proposed $1.1 billion deal for Enobia Pharma Inc. by **Alexion Pharmaceuticals Inc.** (NASDAQ:ALXN), which is expected to close in 1Q12.

Twenty-seven public company acquisitions were completed for an aggregate of $56 billion, the second highest since 2009 when Genentech Inc. was acquired by **Roche** (SIX:ROG; OTCQX:RHHBY) for $46.8 billion. Last year, **Sanofi** (Euronext:SAN; NYSE:SNY) completed its acquisition of Genzyme for up to $23.9 billion, including the value of a contingent value right. The 2011 tally does not include the proposed $11 billion deal for **Pharmasset Inc.** (NASDAQ:VRUS) by **Gilead Sciences Inc.** (NASDAQ:GILD), which is expected to close in 1Q12.

The data include completed acquisitions of companies developing and/or selling therapeutics, and exclude deals in the agbio, diagnostics, generics, supply/service and veterinary segments, as well as reverse mergers, acquisitions of big pharma, and acquisitions of divisions/subsidiaries. Deal values include milestones. (A) The total number of deals displayed below includes those with undisclosed values



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