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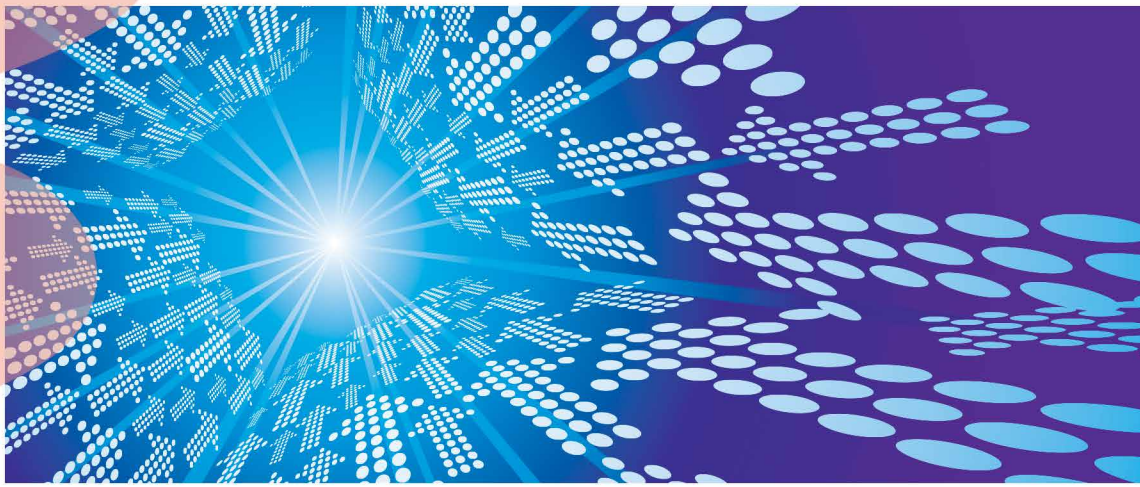
PHARMA & BIOTECH 2013 IN REVIEW



EvaluatePharma®

PHARMA & BIOTECH IN 2013

If there had been any question about the sustainability of the life science sector's recovery in 2012 it was firmly answered in 2013. The Nasdaq biotechnology index ended the year at a record high, US investors became highly receptive to IPOs – even the more high-risk propositions – and secondary fundraisings no longer caused shareholders to flee in alarm at being asked for more money.

By any measure the US public markets last year painted a picture of rude health for life science companies, from the smallest biotech to the largest drug maker. There were of course clinical and regulatory disappointments and surprises, and the bounce back in Europe was more measured, as is typically the case. But US investor enthusiasm for the sector prompted a surge in valuations across the industry.

Partly as a result, the amount spent on M&A grew substantially, even as the number of transactions dipped. Much of the consolidating activity was left to the specialty pharma sector as big pharma continued to stay away from these transactions, preferring to share the risk with partnership deals. The increasing complexity of both takeover deals and licensing transactions – with features like contingent milestones now the norm – shows how distributing the burden of risk remains a high priority for the buyers in the market.

BY ANY MEASURE THE US PUBLIC MARKETS LAST YEAR PAINTED A PICTURE OF RUDE HEALTH FOR LIFE SCIENCE COMPANIES, FROM THE SMALLEST BIOTECH TO THE LARGEST DRUG MAKER.

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Still, prices negotiated in licensing deals did hold up last year, although activity again appeared to dip. With refinancing possible this could well have attracted the focus of many traditionally deal-hungry small companies. What was clearly evident were the numerous broad and far-reaching research collaborations struck between early-stage drug researchers and the big beasts of the industry, as part of an ongoing drive for R&D externalisation.

In the private sphere venture financing stabilised after a couple of difficult years, although with a big proportion of the cash raised going to late-stage companies it was clear that many VCs had their eye on the IPO market and the promise of an exit.

The buoyancy of 2013 has shown no sign of deflating in the first few months of 2014. Surging financial markets are providing a boost, of course, but growing confidence that the industry has started to fix the productivity problems that so concerned companies and investors a few years ago is helping. Having a significant patent cliff in the rearview mirror is another bonus, while the FDA has obliged by making the drug approval process more predictable.

THE BUOYANCY OF 2013 HAS SHOWN NO SIGN OF DEFLATING IN THE FIRST FEW MONTHS OF 2014.

PHARMA & BIOTECH IN 2013

Last year, the US regulator approved eight products painted as future blockbusters, and the crop of new molecules that reached the market are forecast to become the most valuable cohort in at least a decade. This year also promises to yield strong stories about the industry's capabilities. The launch of Gilead's oral hepatitis C therapy Sovaldi, which is expected to smash drug launch records, could well set the tone.

Few were willing to use the word bubble in 2013, but as share prices climb ever higher this will be heard more often. As such, the biggest question mark for the sector in 2014 will be the sustainability of these valuations.

Unless stated, all data are sourced to EvaluatePharma and were accessed in January 2014.

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INVESTOR EXUBERANCE REWARDED

In a year marked by a clear recovery in global equities, drug stocks rewarded investors more than most. Pharmaceutical and biotechnology companies outperformed wider indices in most regions, and none more markedly than in the US.

The performance of the Nasdaq Biotechnology Index stands out among the others. Its previous peak hit during the genomics bubble of 2000 was already surpassed by March, and the index went on to end the year 66% higher.

"It is the generalist investors that arrived late and are indiscriminately investing in biotech stocks that are driving the market now," says Andy Smith, chief investment officer of Mann BioInvest. "Fundamentals are not the driving force. A lot of it stems from the hope that big pharma needs products and therefore they will buy biotechs willy nilly."

Percentage Change in Stock Indices Over 2013

Stock Index	% Change in 2013
NASDAQ Biotechnology (US)	66%
TOPIX Pharmaceutical Index (Japan)	37%
S&P Pharmaceuticals (US)	31%
DJIA (US)	26%
Dow Jones STOXX Healthcare (EU)	20%
Euro STOXX 50 (EU)	14%

Japan saw its own biotech bubble take shape last year, spurred on by a Nobel prize for the country's top stem-cell researcher and a promise of billions of yen of research funding from the government. This kick-started a surge in valuations for the country's life science companies, outdoing the performance of European groups over the year.

Notably, companies of all sizes benefitted from investor exuberance last year. While several smaller stocks saw many-fold increases in their valuations larger companies made advances that, percentage-wise, are not normally seen in this stock category.

Two facts illustrate the extent of investor support. No drug maker worth more than $30bn at the beginning of 2013 shrank in value over the year. And, during this period, these companies added a combined $531bn to their market capitalisations.

A look at the best and worst performers in this group shows how the industry's big biotechs got even bigger – Celgene, Gilead and Biogen Idec all pretty much doubled in value.

"In a low interest rate environment, you want to look for companies that can return double digit sales and earnings growth. And that is the big biotechs," says Mr Smith.

Gilead ended the year worth $115bn, a lot more than traditional big pharma names like Bristol-Myers Squibb, AstraZeneca and Eli Lilly, which were worth $88bn, $75bn and $57bn respectively at year end.

Even the sector's laggard, Lilly, managed to squeeze out a 3% gain. However, considering the sector's performance last year, no company should have been happy with a single-digit advance.

Big Cap Top Risers and Fallers in 2013

		Share Price (local currency)			Market Capitalisation ($bn)	
Rank	**Top 5 Risers**	**31-Dec-12**	**31-Dec-13**	**Change**	**31-Dec-12**	**31-Dec-13**
1	Celgene ($)	78.47	168.97	115%	33.19	69.63
2	Gilead Sciences ($)	36.72	75.10	105%	55.65	115.15
3	Biogen Idec ($)	146.37	279.57	91%	34.63	66.04
4	Bristol-Myers Squibb ($)	32.59	53.15	63%	53.80	87.51
5	Abbvie ($)	35.12	52.81	50%	55.87	84.01
Rank	**Top 5 Worst Performers**					
1	Eli Lilly ($)	49.32	51.00	3%	55.57	57.46
2	Baxter International ($)	66.66	69.55	4%	36.62	37.74
3	Teva Pharmaceutical Industries ($)	37.34	40.08	7%	35.23	37.95
4	Sanofi (€)	71.39	77.12	8%	122.65	139.31
5	Novo Nordisk (DKr)	916.50	994.00	8%	72.14	80.47

But, for confirmation of just how richly biotech stocks rewarded investors last year, a look at the biggest movers among the smaller players reveals all.

Endo was one of several companies applauded by investors last year for piling on the debt and striking a big acquisition. Investor reaction to its move on Paladin Labs was unanimously positive, and similarly effusive reactions were seen after deals struck by the likes of Actavis, Jazz and Perrigo, all of which were motivated in part by gaining assets in lower tax jurisdictions. Such shareholder reactions will do nothing if not encourage more M&A moves like these this year.

The fivefold-and-then-some advances of the likes of Puma and Acadia were remarkable on any measure, particularly considering that neither of these one-asset companies has actually got its respective product on the market yet. Investors are betting that potential buyers will also see the value they have implied for these therapies.

That Isis was one of the best performing stocks last year really illustrates the extent of investor enthusiasm. As a platform company working with RNAi-based therapies – a structure not traditionally favoured by investors and a field that has struggled to prove its value over the years – Isis's resurgence is a testament to the willingness of shareholders to embrace cutting-edge technologies once again.

Finally, Inovio is a beneficiary of interest in what has become the hottest R&D field – immuno-oncology – and a deal with Roche sealed its place in this arena.

Of course for an industry where failure is always possible setbacks still happened, both on the market and in the clinic. Ariad, Affymax and Amarin proved that winning their respective approvals was far from the end of the game. The leukaemia drug Iclusig was let back on the market, but has been severely damaged by safety issues, anaemia treatment Omontys was withdrawn for good on safety concerns, while the triglyceride-lowerer Vascepa continues to disappoint. Aveo's kidney cancer project tivozanib did not even make it that far, and was nixed by the FDA, while Resverlogix failed in a second attempt to prove that its HDL boosting therapy actually works.

Other Significant Risers and Fallers in 2013

		Share Price (local currency)			Market Capitalisation ($m)	
Rank	**Notable Risers**	**31-Dec-12**	**31-Dec-13**	**Change**	**31-Dec-12**	**31-Dec-13**
1	Endo Health Solutions ($)	26.23	67.46	157%	2,993	7,747
2	Isis Pharmaceuticals ($)	10.44	39.84	282%	1,204	4,624
3	Puma Biotechnology ($)	18.75	103.53	452%	537	2,970
4	ACADIA Pharmaceuticals ($)	4.65	24.99	437%	413	2,271
5	Inovio Pharmaceuticals ($)	0.50	2.90	481%	70	604
Rank	**Notable Fallers**					
1	ARIAD Pharmaceuticals ($)	19.18	6.82	(64%)	3,197	1,266
2	Amarin ($)	8.09	1.97	(76%)	1,096	340
3	Affymax ($)	18.99	0.78	(96%)	706	29
4	AVEO Oncology ($)	8.05	1.83	(77%)	352	95
5	Resverlogix (C$)	1.60	0.49	(70%)	120	38

Ranked on Market Cap.

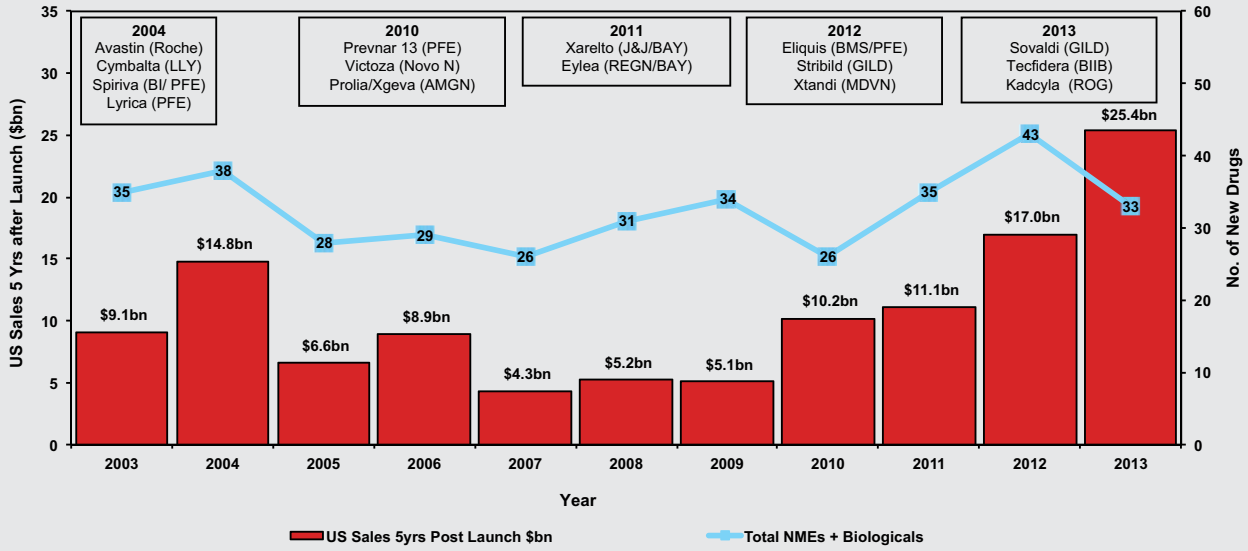
Notable Risers	**EP Vantage Comment and Analysis**
Endo Health Solutions	Endo engineers Paladin into a return for all
Isis Pharmaceuticals	ADA - Knockdown result boosts Isis and antisense alike
Puma Biotechnology	Puma roars but neratinib's real value remains opaque
ACADIA Pharmaceuticals	Possibility of earlier pimavanserin approval boosts Acadia
Inovio Pharmaceuticals	Immuno-oncology buzz awakens Roche's interest in cancer vaccines
Notable Fallers	
ARIAD Pharmaceuticals	Future darkens further for Ariad on news of trial termination
Amarin	Clock ticks for Amarin as outcomes awaited
Affymax	Affymax faces extinction after Omontys debacle
AVEO Oncology	Adcom double play erases Aveo and Delcath
Resverlogix	Resverlogix doomed by second failure

2013: THE YEAR OF EIGHT BLOCKBUSTERS

A strong run of novel and highly valuable drug approvals has only encouraged heady investor enthusiasm for the sector.

The FDA actually approved fewer novel molecules last year than in 2012 – a record year that prompted widespread back slapping and claims of improved R&D prowess – but the value of 2013's cohort was record-breaking in its own right. According to EvaluatePharma, combined fifth-year projected sales are forecast to hit $25.4bn, the highest in the last decade by a long way, and 50% more than even 2012's 43 new drugs.

FDA Approval Count vs. Total USA Product Sales 5 Years After Launch



Eight of the drugs approved last year are considered to be blockbusters-in-waiting, led by the likes of Gilead's hepatitis C pill Sovaldi, Biogen Idec's oral MS therapy Tecfidera and Roche's antibody-drug conjugate Kadcyla, which are considered to have multi-billion dollar sales potential.

Still, market-disrupting drugs like these do not come along every year. Although a couple of big approvals are on the horizon, such as Merck & Co's anti-PD-1 antibody MK-3475, 2014 will struggle to match last year's R&D output in terms of value. Investors assuming that measures of the industry's productivity such as these will continue to grow at this rate could well be disappointed.

"As the FDA continues to approve drugs at a good clip, we won't see as many block-busters," Mr Smith says. "And we could see more drugs approved that never support the amount of spend to get there, or the cost of being a public company."

However, investor concerns about the regulatory climate have lessened in the last few years, Mr Smith says, and the FDA's efforts to improve collaboration and communication have been widely applauded.

10 Biggest Approved Drugs of 2013

Rank	Product	Generic Name	FDA Approval Date	Company	2018e Annual Sales US ($m)
1	Sovaldi	sofosbuvir	December 06	Gilead Sciences	5,221
2	Tecfidera	dimethyl fumarate	March 27	Biogen Idec	3,299
3	Kadcyla	ado-trastuzumab emtansine	February 22	Roche	3,049
5	Imbruvica	ibrutinib	November 13	Pharmacyclics	2,453
4	Tivicay	dolutegravir	August 12	GlaxoSmithKline	2,132
6	Breo Ellipta	fluticasone furoate; vilanterol trifenatate	May 10	GlaxoSmithKline	1,332
7	Anoro Ellipta	umeclidinium bromide; vilanterol trifenatate	December 18	GlaxoSmithKline	1,242
9	Gazyva	obinutuzumab	November 01	Roche	1,149
8	Brintellix	vortioxetine	September 30	Takeda	875
10	Xofigo	radium Ra-223 dichloride	May 15	Bayer	829

The famously cautious US regulator has become more predictable and timely in its decisions, and these attributes always go down well with investors. The implementation of its new breakthrough therapy designation is a case in point. This is granted to projects being developed in specific indications deemed to be of high unmet need, and those that have received approval so far reached the market in record speed – in only four months in the case of Pharmacyclics' Imbruvica in mantle cell lymphoma.

This is not to say that the FDA has relaxed its stance on safety, or efficacy in cases where the product is addressing a less urgent gap in the market. Diabetes drugs for example continue to attract much scrutiny, while the onus on proving a benefit for cardiovascular medicines destined to be used by a broad population is more onerous than ever.

It is no wonder that drug makers are increasingly focusing on rare illnesses, and this concentration of efforts has played no small part in the improvement of approval rates over the past couple of years.

BEYOND THE PATENT CLIFF

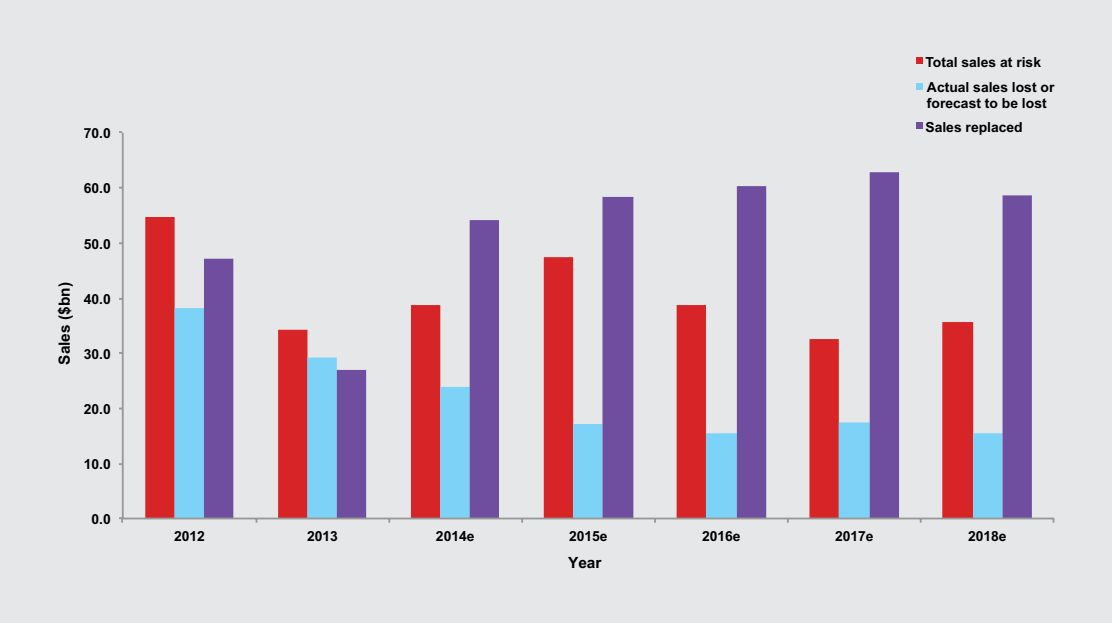
The past few years have seen many of the world's biggest-selling drugs lose patent protection – Pfizer's Lipitor and Sanofi and Bristol-Myers Squibb's Plavix are two major examples – meaning many big pharma companies have already felt the loss of their previous top sellers. This factor has also played a part in helping to improve investor sentiment towards the sector; the collapse in earnings that is still happening at Sanofi, AstraZeneca and Eli Lilly might be hurting, but at least shareholders can start to look beyond these events now.

Some big losses are still on the way – Novartis's Diovan is living on borrowed time and could fall at any time, while the days are numbered for Teva's Copaxone and AstraZeneca's Nexium. Both will see generics enter in May.

However the resilience of off-patent biologics and inhaled products means many of the impending patent losses are unlikely to result in big erosions of sales. EvaluatePharma's consensus forecast data reveals that equity analysts expect only 36% of the sales at risk of generic erosion in 2015 actually to be lost. In 2012, the corresponding number was a huge 70%.

At the same time, analysts expect growth of new and existing products to far outstrip those lost to cheaper copycats in the coming years. It should be remembered that these predictions are based on the assumptions of analysts who tend to be very bullish about the prospects of the industry, particularly in the current climate. But even taking this into account these figures paint a picture of an industry in rude health and help explain why investors are embracing these companies once again.

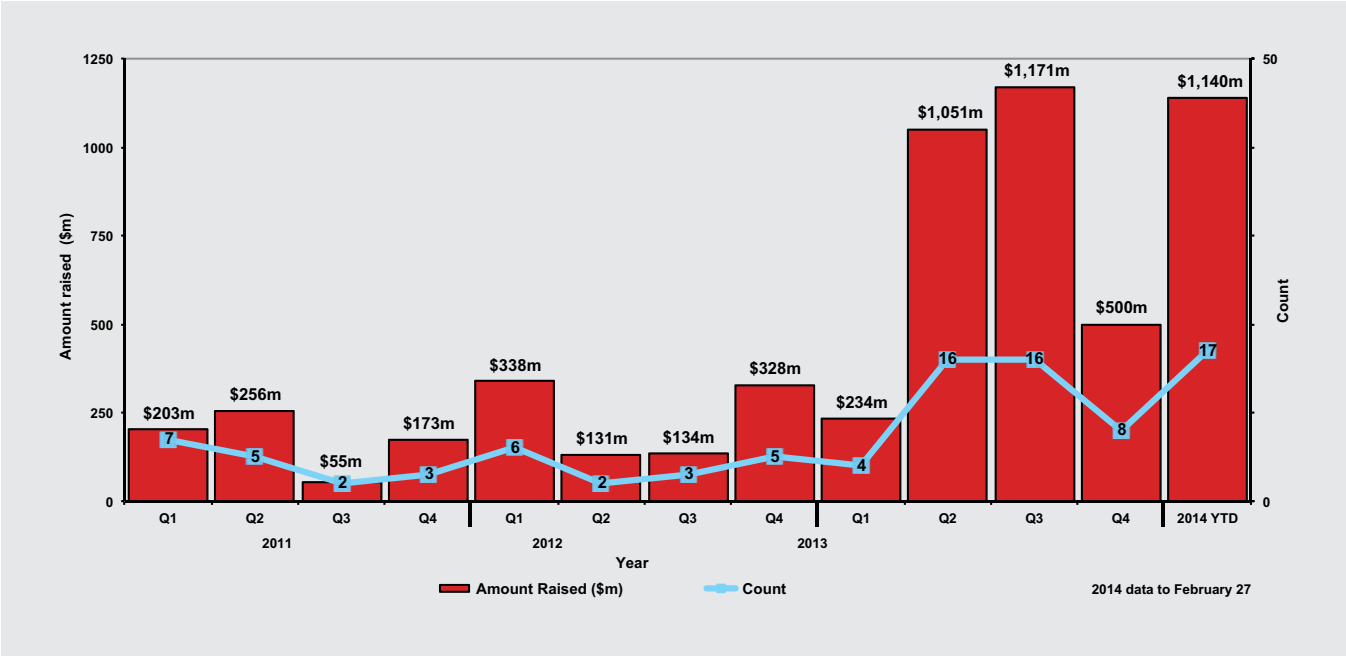
Worldwide Rx and OTC Sales at Risk of Patent Expiry



OPENING OF THE IPO FLOODGATES

Enthusiasm for all things biotech caused the IPO window to be flung wide open last year. New issues, a very rare beast in the wake of the financial crisis, began to emerge at the back end of 2012 and have been picking up pace ever since.

Initial Public Offerings by Quarter on Western Exchanges



Source: EP Vantage

As last year progressed it became far less likely that a company would have to accept a cut to its targeted float price to get investors on board. And several new issues ended the year worth many times more than their IPO valuation. Leading the pack was Insys Therapeutics, which is commercialising a treatment for cancer pain; its stock saw a more than fivefold surge in value last year and has carried on climbing since.

Just nine newly public biotechs saw their value contract by year end. Prosensa led the way after the apparent failure of its lead project, a novel Duchenne muscular dystrophy therapy. In fact the Netherlands-based company was typical of many Europe-based companies that chose to shun the cautious markets of their homelands, and tap less risk-averse US investors.

Still, floats in Europe have been happening and even in the UK, where public investors have very little appetite for early-stage biotechs, a brave biotech decided to test the waters. Should the allergy specialist Circassia raise the $334m it is targeting and receive a warm reception as a public company, it will be hard to argue that sentiment has yet to travel across the Atlantic.

What will test sentiment is the longer-term performance of these companies, many of which are approaching the inflection point on which they floated. And as the window opens to even higher-risk and arguably lower-quality companies, it could become harder to maintain the high-growth reputation of these new issues.

Top 10 Biotech IPOs on Western Stock Exchanges in 2013

Company	Date	Amount Raised	Offering Price	Range	Discount/ Premium	Exchange	2013 YE Change Since Float
Ophthotech Corporation	September 25	$167m	$22	$16-19	26%	Nasdaq	47%
Intrexon Corporation	August 08	$160m	$16	$14-16	7%	NYSE	49%
PTC Therapeutics	June 20	$125m	$15	$13-16	3%	Nasdaq	13%
Portola Pharmaceuticals	May 22	$122m	$14.50	$13-16	0%	Nasdaq	78%
Karyopharm Therapeutics	November 06	$109m	$16	$14-16	7%	Nasdaq	43%
Agios Pharmaceuticals	July 24	$106.2m	$18	$14-16	20%	Nasdaq	33%
Chimerix	April 11	$102m	$14	$13-15	0%	Nasdaq	8%
Bluebird Bio	June 18	$101m	$17	$14-16	13%	Nasdaq	23%
Acceleron Pharma	September 19	$83.7m	$15	$13-15	7%	Nasdaq	164%
OncoMed Pharmaceuticals	July 18	$81.6m	$17	$14-16	13%	Nasdaq	74%
Average across all 44 IPOs		***$67m***			***(13%)***		***59%***

Source: EP Vantage

VENTURE INVESTMENTS STABILISE AS WINNERS INCREASINGLY TAKE ALL

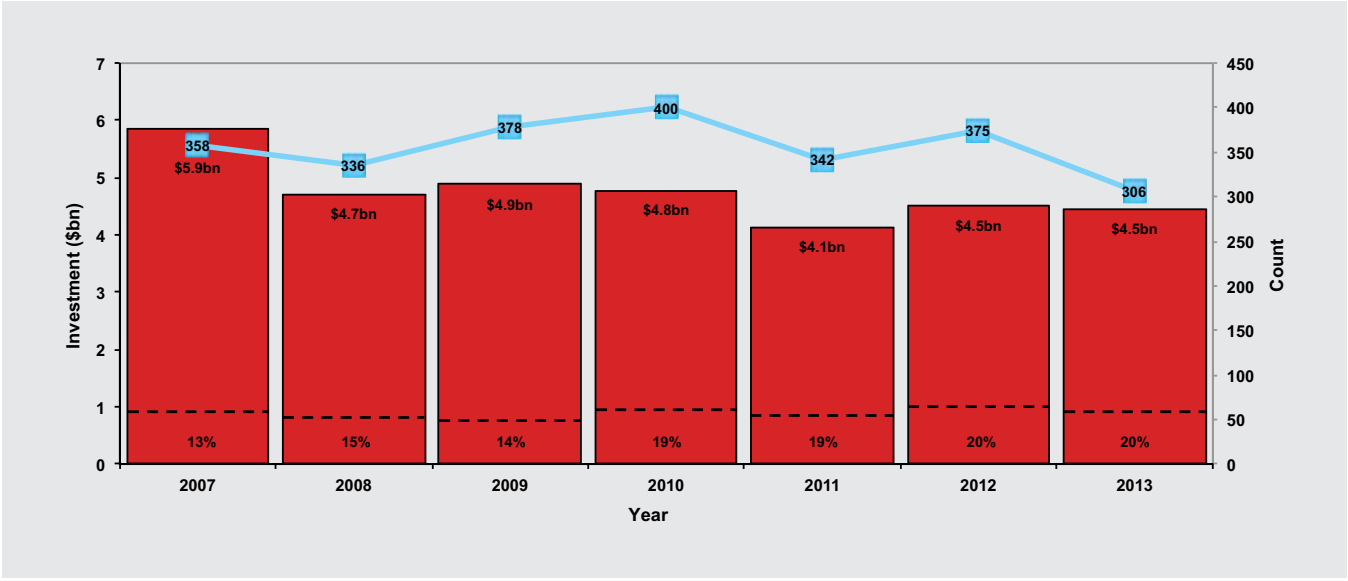
Venture capital firms have also been a big beneficiary of the IPO boom. A flotation still cannot be considered an immediate exit for these early-stage investors, but it is a definitive step towards one. And for years this route has effectively been shut down.

This has contributed to a substantial improvement in the mood at these firms, despite the fact that, for many, their own investors remain cautious and hard to tap for new funds. An improving exit environment is expected to help in this regard, and many predict a pick-up in venture capital investments in 2014.

"You are about to see a huge resurgence in venture capital in healthcare," says Jonathan Silverstein, a partner at US investment firm Orbimed.

"We had about 50 IPOs in the last two years. As those returns filter through to the venture capital firms, you are going to see funds that looked like money losers starting to make money. And then investors will realise they are drastically under-allocated in venture capital."

Annual VC Investments with 10 Biggest Rounds Shown as Proportion of Total Raised



EvaluatePharma data show that in 2013 private drug developers raised $4.5bn from venture funds, a similar amount to 2012 but still an encouraging sign from the end of the sector that really struggled with the fallout of the banking crisis. These data only cover companies developing human therapeutics, and exclude medtech or diagnostic investments.

Less encouraging, perhaps, is the finding that the sum was shared among considerably fewer companies. This suggests that whatever money is available is being focused in greater amounts towards the chosen few, as venture funds seek safety in numbers and attempt to get their portfolio companies as far along their development path as possible.

An analysis of the data reveals that the top 10 venture rounds last year captured 20% of the cash raised by this sector, up from 13% in 2007. The following table, of last year's biggest rounds, shows how the majority of these firms have already moved into the public sphere.

This is all very well if you are one of the chosen few. But this concentration of cash into near term exit opportunities could well impact others looking for funding, and these will tend to be the earlier-stage or higher-risk propositions.

This pattern of investment reflects an industry fighting to convince its own share-holders – the limited partners that invest in venture funds – that attractive returns can be generated, after several years of disappointing performance. At the moment, this means that the risk capital is itself fleeing from the very riskiest.

Should the IPO scene allow many of these venture firms to exit their investments and return healthy profits to their limited partners, this might change. But ongoing support from the public markets is required for this to happen, particularly in the US. Any readjustment in confidence would be a huge blow to the venture capital industry, among others.

Biggest VC Rounds of 2013

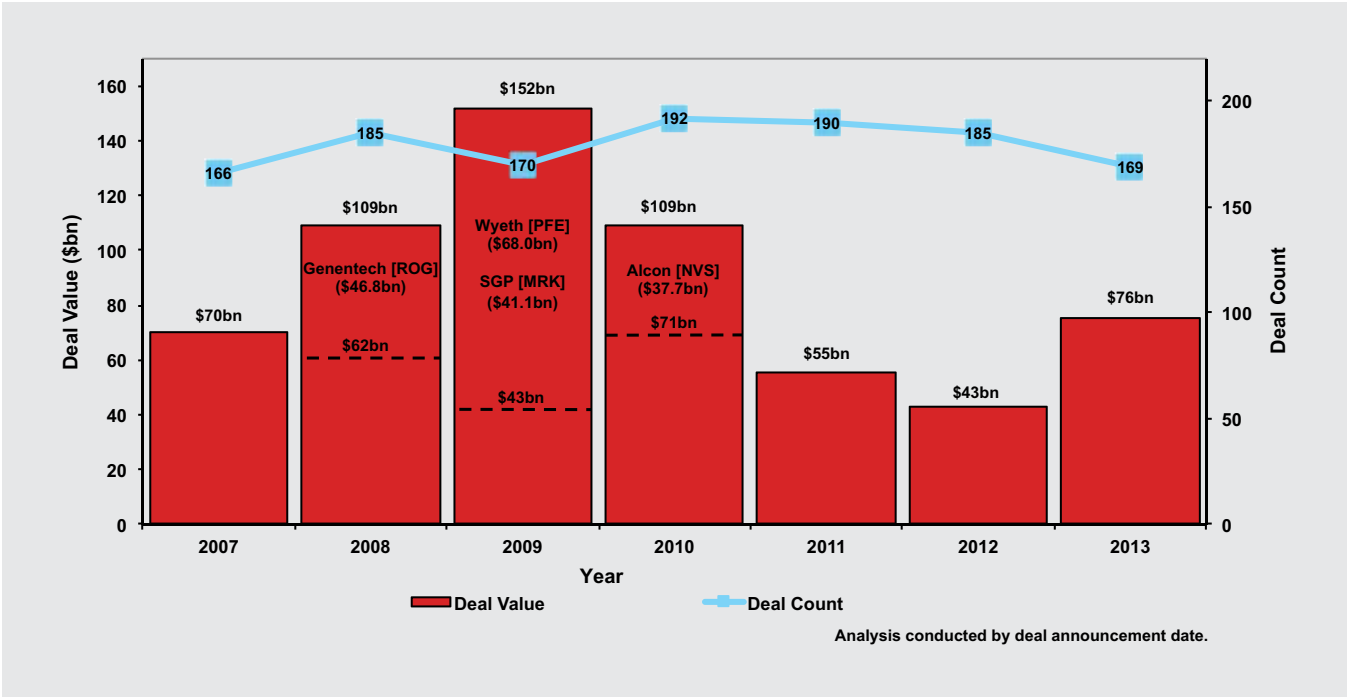
Company	Financing Round	Investment ($m)
Intrexon*	Series F	150.0
Juno Therapeutics	Series A	120.0
Moderna Therapeutics	Series B	110.0
Revance Therapeutics*	Series E	104.0
Ganymed Pharmaceuticals	Series E	64.4
PTC Therapeutics*	Series G	60.0
Dicerna Pharmaceuticals*	Series C	60.0
Trevena*	Series C	60.0
Ophthotech*	Series C	50.0
NGM Biopharmaceuticals	Series C	50.0

*Have floated or signalled an intent to do so

DEAL METRICS CLIMB AS BIG PHARMA STAYS AWAY FROM M&A

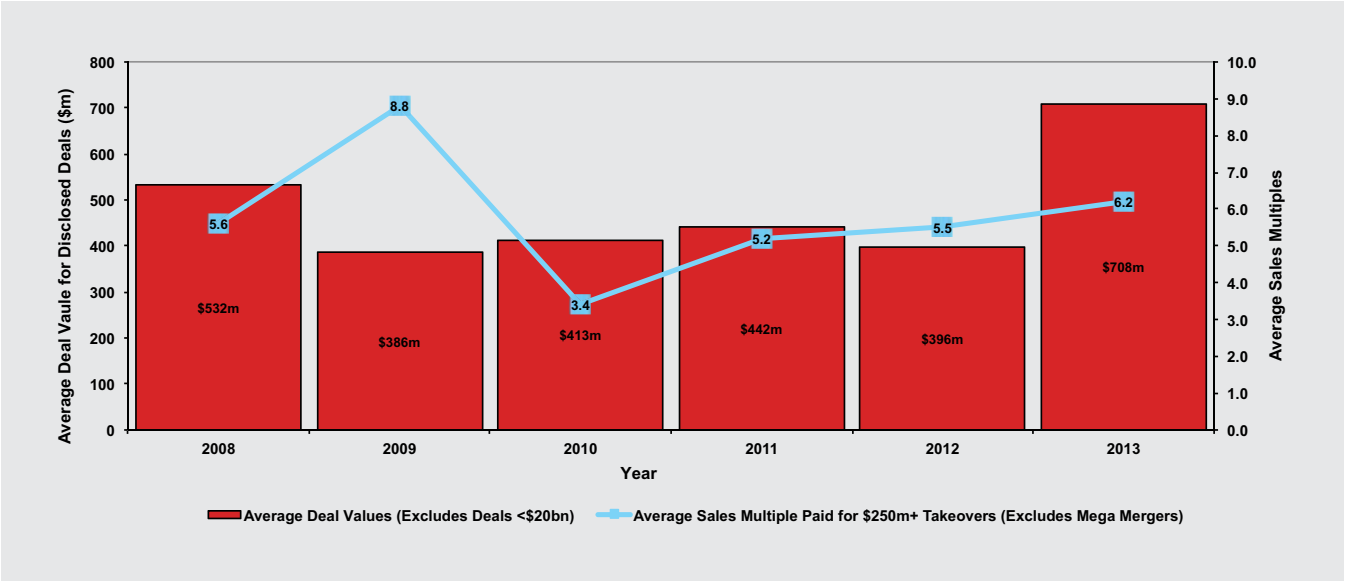
Although venture funds will be welcoming the booming IPO market, the takeout of a portfolio company remains the preferred exit for these investors. And, encouragingly, EvaluatePharma data shows a big jump in the amount of money committed in M&A transactions last year.

Pharma and Biotech M&A Activity



Valuations might be sky high, but this did not seem to deter motivated buyers. The average deal value reached $708m last year, the highest since pre-crash levels, while the average sales multiple paid climbed for the third year in a row.

Average Deal Values and Sales Multiples



A look at who is spending the money, however, paints another picture. Much of the consolidation is happening within the specialty or generics space, with big pharma remaining relatively quiet and the huge valuations of biotechs deterring would-be suitors.

"Most biotech investors are in it for the M&A activity, and they are looking over at specialty pharma and thinking why shouldn't that be biotech? But because the prices are so high no-one is doing anything," Mann Bioinvest's Mr Smith says.

Deal-hungry mid-cap specialty players have a very different strategic outlook to the sort of company that might consider buying a high-risk, cash-burning biotech. Fuelled by cheap debt and motivated by the desire to add scale and cash flow, the spending spree on which the likes of Valeant, Endo and Actavis have embarked shows no signs of slowing.

Big pharma, meanwhile, commits a lot of money to product and research deals, and their own R&D efforts, so they are certainly not hoarding cash. But it is clear that many of these companies now prefer to pursue a collaborative relationship with potential targets, rather than committing to a takeout.

Sky-high asset prices will not be helping to change their mind on this. Luckily, big biotech has stepped in to a certain extent. But big pharma's disinterest has to be disappointing – and concerning – to public and private investors focused firmly on a takeout.

The Industry's Big Spenders Top 10 – Three-Year M&A Bill

M&A ranking	Company	3 Year Spend ($bn)	3 Year Deal Count
1	Johnson & Johnson	21.4	11
2	Actavis	15.7	6
3	Valeant	15.2	18
4	Takeda	14.9	7
5	Amgen	14.2	7
6	Gilead Sciences	12.3	4
7	Bristol-Myers Squibb	10.0	3
8	Perrigo Company	9.9	7
9	Teva	8.4	7
10	Fresenius	7.0	13
	Total Big Pharma	*44.0*	*56*

Top 5 Pharma/Biotech M&A Deals in 2013

Rank	Acquiring Company	Target Company or Business Unit	Deal Value ($bn)
1	Amgen	Onyx Pharmaceuticals	10.4
2	Valeant Pharmaceuticals International	Bausch + Lomb	8.7
3	Perrigo Company	Elan	8.6
4	Actavis	Warner Chilcott	8.5
5	AstraZeneca	Diabetes business of Bristol-Myers Squibb	4.3

BROAD RESEARCH DEALS DOMINATE AS LICENSING ACTIVITY DIPS

Licensing deals are frequently described as the lifeblood of the industry, and EvaluatePharma data show a dip in the number of products changing hands via these transactions last year. On the upside, rising asset prices appear to have helped keep deal values healthy.

A slowdown in product deals could be explained by the fact that big pharma, the traditional licensing-hungry partner, has largely calmed its patent cliff fears with a frantic few years of deal making. And smaller companies might be choosing to take advantage of the availability of financing options while they can, and retaining assets for longer.

Annual Product Deals – Total Deal Values, Up-fronts and Product Count

What is clear is the growing popularity of overarching research collaborations, frequently struck over technologies before they move into human testing. Six of the 10 biggest deals struck last year were essentially broad, pre-clinical technology platform deals that will see the smaller company take on specific research work.

These types of deal are a sure sign that the externalisation of R&D that big pharma is enthusiastically pursing is continuing apace.

Five Biggest Deals in 2013 – Ranked by Up-front Payment

Rank	Company	Deal Partner/ Product Source	Lead Product or Programme	Status on Deal Date	Therapeutic Category	Up-front Payment ($m)	Deal Value ($m)	Deal Type
-	*Biogen Idec*	*Elan*	*Tysabri*	*Marketed*	*MS therapy*	*3,250*	*3,250*	*Product acquisition*
1	Sellas Life Sciences Group	Fosun International	Fotagliptin Benzoate and Pan-HER Inhibitor	Pre-clinical	Anti-diabetic and cancer inhibitor	518	518	In-licensed
2	AstraZeneca	FibroGen	Roxadustat	Phase III	Anti-anaemic	350	815	In-licensed
3	AstraZeneca	Moderna Therapeutics	AstraZeneca/Moderna Cancer Project	Research project	Anti-cancer therapy	240	420	Out-licensed technology
4	Forest Laboratories	Merck & Co	Saphris	Marketed	Anti-psychotic	240	240	In-licensed
5	Celgene	FORMA Therapeutics	FORMA/Celgene Research Program	Research project	Anti-cancer therapy	200	515	In-licensed

Five Biggest Deals in 2013 – Ranked by Deal Value

Rank	Company	Deal Partner/ Product Source	Lead Product or Programme	Status on Deal Date	Therapeutic Category	Up-front Payment ($m)	Deal Value ($m)	Deal Type
-	*Biogen Idec*	*Elan*	*Tysabri*	*Marketed*	*MS therapy*	*3,250*	*3,250*	*Product acquisition*
1	Celgene	OncoMed	Demcizumab	Phase II	Cancer antibody	155	3,332	In-licensed
2	Eli Lilly	Pfizer	Tanezumab	Phase III	Pain antibody	200	1,780	In-licensed
3	Roche	Molecular Partners	Roche/Molecular Cancer Program	Research project	Anti-cancer therapy	60	1,156	In-licensed
4	Gilead Sciences	MacroGenics	Gilead/MacroGenics DART Program	Research project	Cancer antibody	30	1,115	In-licensed
5	Roche	immatics biotechnologies	IMA942	Pre-clinical	Cancer vaccine	17	1,017	In-licensed

What these top-line numbers do mask, however, is the growing complexity of these deals, driven by the ongoing desire of bigger partners to share the risk of these projects.

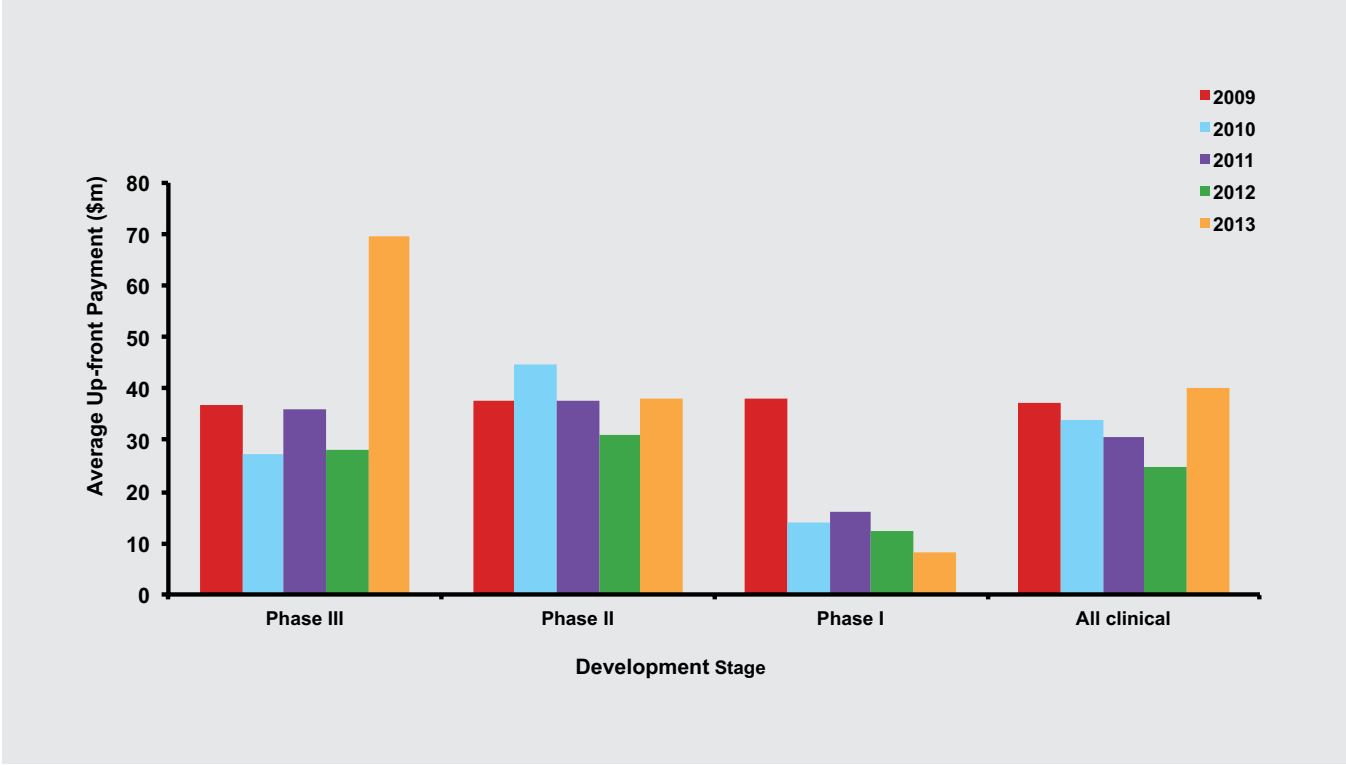
"Whether it's royalties or additional milestone payments, the deals I'm seeing are more structured where the up-front is a smaller aspect of the deal," says Adam Golden, a partner at law firm Hogan Lovells.

"The collective experience of the industry is such that people are really reluctant to swallow big up-fronts and are pushing to make payments more back ended, with higher royalties."

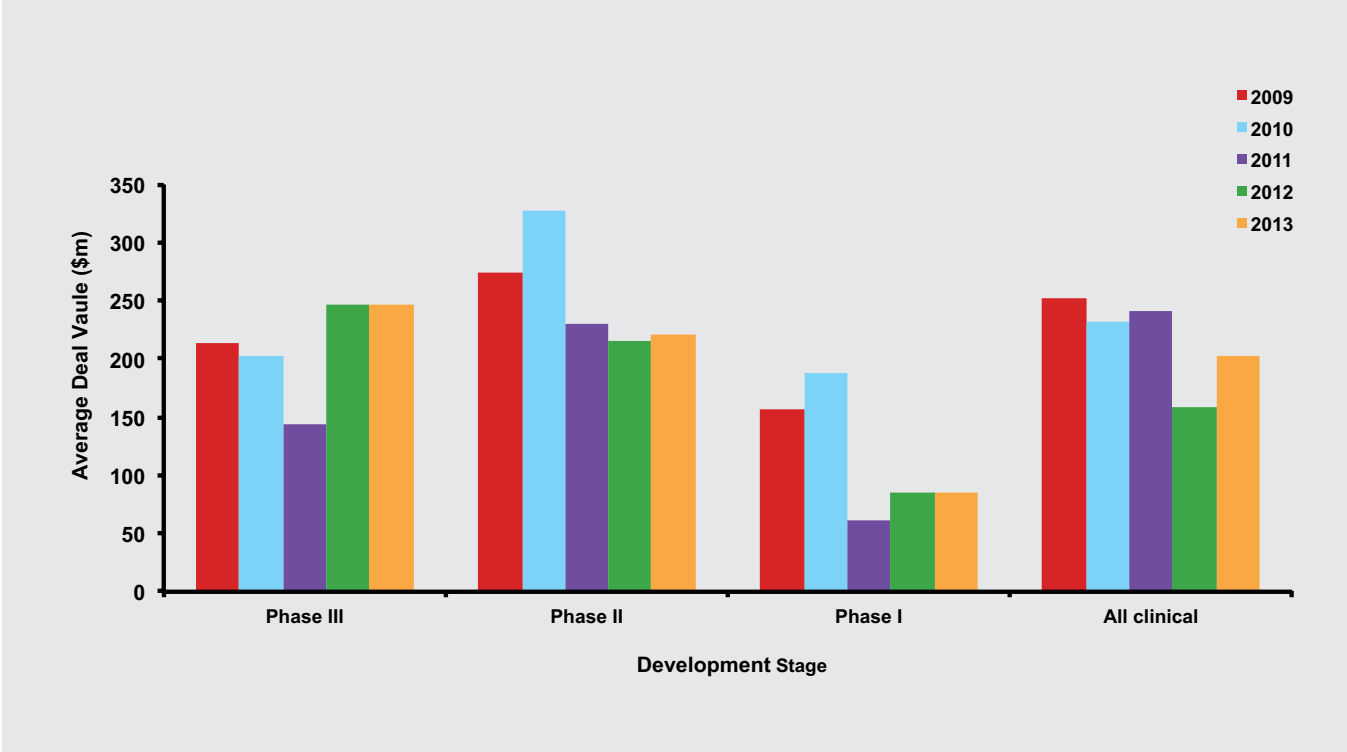
Highly structured deals are likely to continue as commonplace, Mr Golden believes, in M&A transactions as well as in licensing.

"I struggle to think of an M&A deal that I have worked on recently that didn't involve some sort of contingent payment. It's an easy way to bridge gaps in valuations, and to increase the headline price. It's part of the DNA of these deals now," he says.

Average Up-front Payment ($m) per Development Stage



Average Deal Value ($m) per Development Stage



NO SIRENS YET

Last year, public investors – in the US at least – showed a huge willingness to embrace the trials and tribulations of drug development, with few listed companies failing to benefit from the exuberance of the stock market. At the same time many private investors remained much more risk averse, carefully picking their investments to maximise the chances of a quick exit.

Meanwhile, the big partners sitting around the deal tables are proving to be very risk aware. They are clearly willing to take bets on some very novel technologies, but have developed the structures to reduce their exposure to failure. Their desire to tap into innovations happening outside their own labs is still being tempered by the demands of their own investors to prove that the days of indiscriminately splashing the cash are over.

So it seems likely that big pharma will refuse to buy into the soaring valuations being enjoyed by many a biotech executive in the US, and will continue to prioritise risk sharing over risk taking. It will be telling of a buyer's desperation if any of the highly valued single-product companies fingered for a bid succumb while asset prices are so high.

Few will be wishing an end to the biotech bull run, but it will happen. There were very few big surprises or setbacks in 2013 to serve to remind investors of the risks inherent in drug discovery, and 2014 is shaping up to tell some successful stories.

While equity markets in the US and Europe remain strong, many believe the biotech sector will be able to retain its allure.

"You don't want to be the first one to leave a party, but you want out before the cops arrive. And I can't hear any sirens yet," says Mr Smith.

Perhaps the real test of investors' faith in the sector will come when, for whatever reason, the wider markets become more risk averse.

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