

Small cap biotechs reap rewards of the bull market in 2013



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For confirmation of just how richly biotech stocks rewarded investors last year, a look at the biggest market movers among the industry's smaller players reveals all. In the US alone, 22 small cap drug developers saw their market values more than double, with many of these enjoying three or even fourfold share price climbs.

Leading the small cap companies - defined by *EvaluatePharma* as those with a market value of between \$250m and \$2.5bn - were Puma Biotechnology and Acadia; their share prices surged more than fivefold over the year. But of course even a bull run has its share of disasters, and the likes of Affymax, Pharmaxis and Celsion will not be remembering 2013 as fondly (see tables below).

Small cap (\$250m-2.5bn) pharma companies: top risers and fallers in 2013

Rank	Top 5 risers	Share price (local currency)			Market capitalisation (\$m)		EP Vantage comment and analysis
		YE 2012	YE 2013	Change	YE 2012	YE 2013	
1	Puma Biotechnology	\$18.75	\$103.53	452%	537	2,970	Puma roars but neratinib's real value remains opaque
2	ACADIA Pharmaceuticals	\$4.65	\$24.99	437%	413	2,271	Possibility of earlier pimavanserin approval boosts Acadia
3	Isis Pharmaceuticals	\$10.44	\$39.84	282%	1,204	4,624	ADA - Knockdown result boosts Isis and antisense alike
4	Clovis Oncology	\$16.00	\$60.27	277%	483	2,043	Asco - Clovis price is twice as nice following double cancer win
5	Celldex Therapeutics	\$6.71	\$24.21	261%	543	2,133	Celldex and ImmunoCellular fall and rise on hype and hope
Rank	Top 5 fallers						
1	Affymax	\$18.99	\$0.78	(96%)	706	29	Affymax faces extinction after Omontys debacle
2	Pharmaxis	AUS\$1.24	AUS\$0.11	(92%)	394	31	Weekly Market Movers (to 1 Feb 2013)
3	Celsion	\$36.86	\$3.89	(89%)	287	16	Celsion bereft after ThermoDox failure
4	AVEO Oncology	\$8.05	\$1.83	(77%)	352	95	Adcom double play erases Aveo and Delcath
5	Amarin	\$8.09	\$1.97	(76%)	1,096	340	Clock ticks for Amarin as outcomes awaited

Yesterday's analysis of the market moves registered last year by the world's largest drug makers revealed that

not one \$30bn+ stock fell in 2013, thanks to the resurgence of interest in healthcare stocks being accompanied by a wider recovery of equity markets ([*Biotech bull run leaves few big cap drug stocks down in 2013, January 7, 2014*](#)).

But the clamour for all things biotech is more clearly demonstrated by the performance of these smaller drug developers, which operate at the high-risk end of the sector. These frequently have a thin pipeline or just one product in the lab, many years from the market, and development risk is amplified by the constant quest for financing.

Such cash-hungry companies are typically the territory of specialist investors. The entry of generalist investors has helped inflate share prices in the US and no doubt fuelled the staggering share price gains enjoyed by the groups highlighted in the analysis below, and more behind them. Many still have much to prove, the year's biggest gainer, Puma, being a case in point.

A one-product company, Puma is waiting for a swathe of data on neratinib to emerge this year that should paint a more accurate picture of the potential of the pan-Her tyrosine kinase inhibitor in breast cancer. The group's current market value suggests that great things are expected.

The same can be said for Clovis, which has a marginally broader pipeline, with three products in mid to late-stage development awaiting validation, and Celldex, which has a very high-risk glioblastoma cancer vaccine in phase III.

Acadia is slightly ahead with a product ready for filing; pimavanserin should be sent to the FDA later this year, and expectations of a deal or a takeout have driven the stock higher. Meanwhile, Isis is certainly the most substantial company to make the top five risers - with a broad pipeline of in-house and partnered products based on its RNAi technology, and one already on the market being sold by Sanofi, it is perhaps most worthy of the substantial surge in valuation seen this year.

A host of companies follow these top five risers with substantial gains over 2013. Of the 266 small cap companies in *EvaluatePharma's* global universe, 200 registered share price rises over the year. But of course by their very nature not all of these high-risk ventures will succeed, and the biggest disappointments of the year highlight the pitfalls.

Both Amarin and Affymax managed to get products on the market, but ultimately failed to grasp commercial success. Amarin has not managed to convince regulators to grant its lipid-lowering pill Vascepa broad approval, while Affymax's Omontys has been withdrawn owing to safety issues.

Pharmaxis and Aveo fell at the regulatory hurdle, with FDA rejections for their candidates, and Celsion was wiped out even earlier, with the phase III failure of its lead treatment for liver cancer.

Micro caps

Among the industry's tiniest players, investors were still willing to look for potential winners. Plucked from relative obscurity were Lannett, BioCryst, Inovio and Chelsea Therapeutics; only the first, the generics firm Lannett, is a company with sales and profits, and its stock made steady progress over the year.

Japan Tissue Engineering, meanwhile, is a surviving beneficiary of Japan's own biotech bubble, which dominated the risers earlier this year but has since been outdone by the US performance.

Inovio's focus on immunology - a red hot area of research right now has benefited the company, and culminated in a deal with Roche this year. And BioCryst and Chelsea have both managed to recover from previous setbacks.

It is hard to see the top fallers in this group staging a recovery, however. Savient is in the process of winding down, after selling its assets for a rock bottom valuation in the wake of the catastrophic commercial failure that was its gout treatment Krystexxa. The UK's Ark is working towards a similar fate after clinical failure of its gene therapy projects in recent years.

Enzon has seen investors desert after paying a substantial special dividend, and a disappointing performance from a number of products for which it receives royalties. Despite Resverlogix's persistence with its heart project, the company seems unlikely to recover from a second clinical failure, while Delcath's rebuff by an adcom for its lead product will be hard to come back from.

Selected <\$250m pharma companies: top risers and fallers in 2013

Rank	Top 5 risers	Share price (local currency)			Market capitalisation (\$m)		EP Vantage comment and analysis
		YE 2012	YE 2013	Change	YE 2012	YE 2013	
1	Lannett Company	\$4.96	\$33.10	567%	141	1154	
2	Chelsea Therapeutics	\$0.76	\$4.44	484%	51	343	FDA's short-term view helps Chelsea rise from the ashes
3	Japan Tissue Engineering (J-TEC)	¥72,500	¥422,500	483%	168	794	
4	Inovio Pharmaceuticals	\$0.50	\$2.90	481%	70	604	Immuno-oncology buzz awakens Roche's interest in cancer vaccines
5	BioCryst Pharmaceuticals	\$1.42	\$7.60	435%	72	449	BioCryst eyes HAE market as Viropharma struggles to innovate
Rank	Top 5 fallers						
1	Savient Pharmaceuticals	\$1.05	\$0.017	(98%)	77	1	Daily Market Movers (15 Oct 2013)
2	Ark Therapeutics	£0.03	£0.003	(89%)	11	1	
3	Delcath Systems	\$1.23	\$0.255	(79%)	92	32	Adcom double play erases Aveo and Delcath
4	Enzon Pharmaceuticals	\$4.43	\$1.16	(74%)	197	51	Daily Market Movers (5 Jun 2013)
5	Resverlogix	C\$1.60	C\$0.485	(70%)	120	38	Resverlogix doomed by second failure

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