

Select small caps stand out amid wider 2016 stock market declines



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Small cap drug developers were certainly not immune to the collapse in investor support that ravaged their larger rivals last year, but at least this section of the industry managed to generate some returns for shareholders. Actelion, Genmab, Exelixis and Tesaro can count themselves as some of the standout success stories on the stock market in 2016.

Of course there are always blow-ups in biotech – step forward Ophthotech, Juno and Alnylam. And with the speciality space also a complete mess – Valeant, Endo and Perrigo combined haemorrhaged \$50bn of market capitalisation over the year – there were plenty of stories of value destruction around to cancel out those enjoying the ride (see tables).

Mid cap (\$5bn-25bn): top risers and fallers in 12 months

	Share price chg	Market capitalisation (\$bn)		EP Vantage comment
		YE 2016	12mth chg	
Top 5 risers				
Actelion (SFr)	58%	24.60	8.06	Why J&J shouldn't buy Actelion
Genmab (DKr)	28%	10.48	2.51	Darzalex inherits mantle as the Harvoni of 2016
Celltrion (KRW)	27%	11.09	3.00	US biosimilar space reaches its Inflectra point
Lundbeck (DKr)	22%	8.40	1.63	Weekly Market Movers: Global Majors & Industry (to 4 Nov 2016)
Otsuka Holdings (¥)	18%	27.34	6.97	
Top 5 fallers				
Endo International (\$)	(73%)	3.67	(10.18)	Daily Market Movers: Global Majors & Industry (6 May 2016)
Juno Therapeutics (\$)	(67%)	2.00	(3.48)	Ash - Relapses spell more CAR-T uncertainty for Juno
Alnylam Pharmaceuticals (\$)	(60%)	3.21	(4.76)	Alnylam failure puts RNAi under the spotlight again
Hanmi Pharmaceutical (KRW)	(53%)	3.15	(3.12)	Boehringer makes olmutinib a Hanmi-back
Perrigo Company (\$)	(42%)	11.93	(9.25)	What Papa might preach to Valeant

The biggest riser in our mid-cap space – those companies valued from \$5bn to \$25bn at the beginning of the year – was the bid target Actelion. With neither Sanofi nor Johnson & Johnson going public with a firm offer, the fate of the Swiss company and its lofty valuation remains in the balance.

Genmab has benefited from growing hopes for its J&J-partnered multiple myeloma treatment Darzalex, and

many believe that the Danish company could find itself similarly the subject of attentions this year. The same theory holds for Exelixis and Tesaro, below in the small caps, which are riding high on clinical successes for Cabometyx in renal cell carcinoma and niraparib in ovarian cancer respectively.

Notably, no US company claimed a space among the top five mid-cap risers, although Seattle Genetics just missed out with an 18% rise, adding \$1.2bn in market cap over the year. Using this as a measure of value creation, the cancer specialist stands out as the only US mid cap company to achieve this accolade last year.

On the flip side, its domestic cousins dominate the mid-cap fallers. While Juno and Alnylam have been laid low by fears of the side effects of their therapies, Endo and Perrigo continue to struggle to justify their debt-fuelled takeover sprees of the past few years.

Small cap (\$250m-5bn): top risers and fallers in 12 months				
		Market capitalisation (\$m)		
	Share price chg	YE 2016	12mth chg	EP Vantage comment
Top 5 risers				
Exelixis (\$)	164%	4,271	2,989	Therapy focus - New kidney cancer data emerge in time for Asco
Tesaro (\$)	157%	7,182	5,084	Esmo - Tesaro enjoys a ta-dah moment
Array Biopharma (\$)	108%	1,482	880	Array plays catch-up in Braf-Mek derby
Ariad Pharmaceuticals (\$)	99%	2,416	1,233	
Theravance Biopharma (\$)	95%	1,656	1,036	
Top 5 fallers				
Ophthotech (\$)	(94%)	172	(2,573)	Ophthotech flop opens up Novartis nightmare scenario
Proteon Therapeutics (\$)	(88%)	54	(253)	Weekly Market Movers: Global Majors & Industry (to 16 Dec 2016)
Northwest Biotherapeutics (\$)	(89%)	32	(224)	Northwest heads for the bulletin boards
Pronai Therapeutics (C\$)	(87%)	45	(285)	Asco event analyser - 2016's winners and losers
Kempharm (\$)	(85%)	43	(244)	Daily Market Movers: Global Majors & Industry (6 May 2016)

Among the small-cap risers, clinical success has driven share price appreciation for Array, which looks set to enter the Braf-Mek space with its own doublet, and regulatory progress will be watched closely this year.

Ariad has staged something of a remarkable recovery given the commercial problems presented by its toxic leukaemia drug Iclusig, although approval of a second product next year is perhaps piquing interest. Similarly for Theravance, investors are apparently looking past the lacklustre performance of its marketed products, including the antibiotic Vibativ, which also comes with serious side-effect warnings, and are instead focusing on a pipeline that should generate much clinical data this year.

Among the fallers, Ophthotech stands out as one of the biggest catastrophes of the year, with the unequivocal failure of its macular degeneration asset Fovista. The loss of \$2.6bn of market cap illustrates the hopes that were attached to this project.

Phase III failure also crushed Proteon, this time in kidney disease, while Pronai lost its lead lymphoma candidate in phase II. Kempharm, meanwhile, made it all the way to the finish line with its opioid-based pain product Apadaz but regulators' refusal to grant an abuse-deterrent claim scuppered its commercial ambitions.

The sorts of setbacks that triggered these falls from grace are not unusual in drug development and similar

stories will undoubtedly emerge this year. What investors will not want to see is the sheer number of stocks ending the year in negative territory: the large-cap pharma and biotech space, particularly in the US, also had a torrid time in 2016 ([Pharma stocks battered in 2016 storm](#), January 4, 2017).

Hopes for an M&A-driven recovery this year are high. Should this not emerge, and if 2017 follows similar patterns, the desertion of investor support will soon begin to take its toll across the sector.

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