

Sector's smaller players show the way



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With the Nasdaq biotech index proving remarkably resilient to sector-specific and macroeconomic problems alike, smart investors will continue to keep an eye out for signs of panic as a leading indicator of an overall collapse of sentiment.

Nothing provides a better guide to the state of play than small and mid-cap companies, whose size makes them particularly exposed to general sector trends. And the good news about the first six months of 2015 is that there is still no canary in the coalmine, notwithstanding a handful of significant fallers that have suffered their own specific setbacks (see tables below).

Rather, the far more important effect is the continued acquisitiveness of the sector's larger players, accompanied by unrelenting interest in biotech stocks from specialist as well as general investors. As long as the big beasts continue to buy, so should investors, as this week's deal between Celgene and Juno suggests ([Celgene goes for broke, June 30, 2015](#)).

Perhaps the most important faller in the mid-cap group is Puma Biotechnology, off 38% on fears that its sole asset, neratinib, will be relegated to an also-ran by borderline efficacy and toxicity. The company has long been seen as overpriced, and the dribbling away of value indicates a realisation that the takeover thesis alone will not sustain it for long.

Mid cap (\$25-5bn): top risers and fallers in 6 months

	Share price (lc currency)			Market cap (\$bn)		Comment
	YE 2014	Q2 2015	Change	Q2 2015	6mth change	
Top 5 risers						
Eisai	¥4672.0	¥8216.0	76%	20.4	7.6	Biogen clears one Alzheimer's hurdle; now comes the tricky bit
Shionogi	¥3125.0	¥4745.0	52%	13.9	3.8	
BioMarin Pharmaceutical	\$90.4	\$136.8	51%	21.9	8.6	BioMarin stands tall with positive achondroplasia data
Hospira	\$61.3	\$88.7	45%	15.3	5.0	Hospira moves the needle for Pfizer spin-out
Chugai Pharmaceutical	¥2964.0	¥4225.0	43%	19.8	4.4	
Top 5 fallers						
Puma Biotechnology	\$189.27	\$116.75	(38%)	3.8	(2.0)	Asco - Puma might have to rely on extended follow-up
Aspen Pharmacare	ZAR 406	ZAR 360	(11%)	13.7	(3.0)	
PT Kalbe Farma	IDR 1830	IDR 1675	(8%)	6.1	(1.0)	
Isis Pharmaceuticals	\$61.74	\$57.55	(7%)	6.9	(0.4)	Weekly Market Movers (to 6 Feb 2015)
Taro Pharmaceutical	\$148.19	\$143.69	(3%)	6.2	(0.2)	

The antisense player Isis also saw continued deflation of its own bubble after failing to make a go of Kynamro, while GlaxoSmithKline's move to sell a significant stake hit the South African generics player Aspen.

A look at the biggest risers reveals the effect of actual takeover activity: Pharmacyclics and Salix have already been eliminated through buyouts, while Pfizer's acquisition of Hospira should be completed in the second half of this year. BioMarin continues to benefit from speculation that its rare disease focus will see it bought out - perhaps by Shire.

Binary outcomes

Eisai is proving to be the way to play the phase I readout of the Biogen-partnered BIIB037, though it is still far from certain whether a therapeutic window can be found for this Alzheimer's project; Biogen itself is up 19% in the first half.

Binary outcomes also ruled for small-cap stocks, sending up Viomed, Heron, Synergy and Galapagos, with the last of these now awaiting a key decision from AbbVie over a full-blown licensing deal. And down on negative data went the gene therapy players Celladon and Avalanche, while Transgene has had to slash jobs after Novartis last year declined to opt into TG4010.

Small cap (\$250m-5bn) pharma companies: top risers and fallers in 6 months

	Share price (lc currency)			Market cap (\$m)		
	YE 2014	Q2 2015	Change	Q2 2015	Change YTD	
Top 5 risers						
ViroMed	KRW 52700	KRW 178300	238%	2,331.7	1,626.4	Daily Market Movers (6 Mar 2015)
Heron Therapeutics	\$10.06	\$31.16	210%	1,072.7	779.2	Heron works Magic to conjure trial win
Galapagos	€ 16.00	€ 45.80	186%	1,925.7	1,311.1	Galapagos moves towards RA deal but a dark horse remains on the horizon
Synergy Pharmaceuticals	\$3.05	\$8.30	172%	830.4	535.7	Synergy relaxes with positive constipation data
Retrophin	\$12.24	\$33.15	171%	1,159.0	832.1	Daily Market Movers (27 May 2015)
Top 5 fallers						
Celladon	\$19.53	\$1.26	(94%)	30.1	(425.0)	Celladon spoils the gene therapy party
Avalanche Biotechnologies	\$54.00	\$16.24	(70%)	414.6	(798.8)	Avalanche crashes down as gene therapy disappoints
Calithera Biosciences	\$20.2	\$7.14	(65%)	128.1	(234.1)	Asco Event Analyzer - 2015's winners and losers
Transgene	€ 7.00	€ 3.99	(43%)	166.2	(175.7)	
Cellceutix	\$4.39	\$2.58	(41%)	303.7	(197.8)	

Retrophin is an interesting case: the group had spiked in the first quarter on US approval of Cholbam, which came with a rare paediatric disease priority review voucher, and prompted the buyout of Cholbam rights from Asklepiion Pharmaceuticals. The circle was squared in May with [Retrophin's sale of the voucher](#) to Sanofi for up to \$245m, and the stock is now up 171% year to date.

Of course, the smaller the company the more widely its shares swing, and thus the best first-half investor return came from some of the tiniest biotechs, such as the resurgent Anthera, up 446% after its lupus project blisibimod passed a phase III futility analysis. However, micro caps are excluded from this particular analysis.

It is noteworthy that no CAR-T players make it into the second quarter's top gainers. Ziopharm (+129%), for instance, has been overtaken by other small-cap peers, while Collectis saw its stock weaken slightly after completing a secondary listing on Nasdaq.

That said, CAR-T is still a hugely popular space, and Celgene's \$1bn bet on Juno will ensure that it remains that way for a while yet. True, the endorsement is another sign that valuations are exceeding the realms of logic, but what is still missing is any indication that says this kind of enthusiasm is about to end.

If companies like Celgene - with its history of smart deal-making - continue to put up the big bucks, the good times could continue for some time yet.

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