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Mid and small caps provide another rocky ride in the second quarter



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Clinical progress - or the lack of it - underpins smaller biotechs' Q2 stock performance.

In the mid-cap world 2018 belongs to Asian companies. Daiichi Sankyo led the sector in terms of share price rise through the first six months, part of a top five that features only one company from outside the Pacific Rim.

Big gains in small-cap companies were mostly down to clinical progress, with Arrowhead leading the way on the strength of RNA interference candidates in hepatitis B and the rare disease alpha-1 antitrypsin deficiency. The losing side was led by Faron, the Finland-based, London-listed drug developer that missed in respiratory disease.

Quizartinib show

It should not be surprising to see the Asian groups doing so well, alongside the nimble biotechs - after all, the only pharma-specific indices to register a gain in the first half have been Nasdaq biotechnology and the Japan-specific Topix pharmaceutical index ([Big biopharma not the best investment so far in 2018, July, 3, 2018](#)).

Daiichi Sankyo, buoyed by progress with its FLT3 inhibitor quizartinib in acute myeloid leukaemia, led the mid caps with a 44% gain that allowed it to add \$9.1bn in valuation.

Sumitomo Dainippon Pharma has multiple irons in the fire, having two CNS assets awaiting FDA decisions and the mid-to-late-stage cancer assets napabucasin and DSP-7888 progressing.

Mid cap (\$5-25bn): top risers and fallers in H1 2018				
	Share price (local currency)		Market capitalisation (\$bn)	
	H1'18	6mth chg	H1'18	6mth chg
Top 5 risers				
Daiichi Sankyo	¥4,237	44%	27.9	9.1
Taisho Pharmaceutical	¥12,970	44%	10.9	3.5
Lundbeck	DKr448.40	42%	14.7	4.7
Sumitomo Dainippon Pharma	¥2,345	40%	8.7	2.7
Celltrion	KRW303,500	37%	35.6	10.6
Top 5 fallers				
Hanmi Pharmaceutical	KRW64,600	(42%)	3.8	(2.7)
Incyte	\$67.00	(29%)	14.2	(5.8)
Exelixis	\$21.52	(29%)	6.4	(2.6)
Alkermes	\$41.16	(25%)	6.4	(2.2)
United Therapeutics	\$113.15	(25%)	4.9	(1.5)

South Korea-based Celltrion benefited from being one of the few pure-play biosimilars companies, having launched copies of Remicade, Herceptin and Rituxan.

The lone entrant from Western markets, Lundbeck, has bounced back from the loss of chief executive, Kåre Schultz, to Teva - last week appointing the Millennium veteran Deborah Dunsire to that post. It also received EU regulatory backing for Rexulti in schizophrenia.

Among the fallers, Incyte's collapse over bad news for IDO inhibition was one of the big stories of early 2018, but it only made the group the second-biggest decliner ([Incyte's epacadostat blow-up leaves a trail of destruction, April 6, 2018](#)). The mid-cap wooden spoon went to South Korea's Hanmi, which has seen investor support diminish as several deals with Western drugmakers unravelled - in the latest setback the Lilly-partnered project poseltinib was discontinued in rheumatoid arthritis in February.

Exelixis suffered from the twin pains of disappointing earnings and a clinical setback in a combination trial of Cotellic plus Tecentriq in colon cancer. Alkermes received a US refusal-to-file letter for its antidepressant ALKS 5461, while United Therapeutics's treprostinil cash cow looks decidedly thinner after the company said an implantable delivery system would not be launched until the end of the year; this came on top of a fall in earnings due to a rise in costs and royalty payouts.

Triple the fun

Small-cap companies are where the biggest gains and losses can be seen in any year, testing investors' tolerance for risk. To make the top-three risers so far in 2018 a company at least had to triple in valuation; the leaderboard was headed by Arrowhead with a 270% gain.

And Mithra, far from being the most innovative company in this cohort, is up on FDA review of its contraceptive ring secreting etonogestrel and ethinyl estradiol, similar to Merck & Co's Nuvaring.

Small cap (\$250m-5bn): top risers and fallers in H1 2018

	Share price (local currency)		Market capitalisation (\$m)	
	H1'18	6mth chg	H1'18	6mth chg
Top 5 risers				
Arrowhead Pharmaceuticals	\$13.60	270%	1,191	916
Mithra Pharmaceuticals	€31.50	207%	1,455	1,039
Madrigal Pharmaceuticals	\$279.69	205%	4,263	2,957
Mirati Therapeutics	\$49.30	170%	1,567	1,074
Crispr Therapeutics	\$58.76	150%	2,773	1,656
Top 5 fallers				
Faron Pharmaceuticals	71p	(91%)	31	(263)
Edge Therapeutics	\$1.03	(89%)	32	(257)
Celldex Therapeutics	\$0.50	(82%)	72	(329)
Aquinox Pharmaceuticals	\$2.65	(77%)	62	(214)
Protagonist Therapeutics	\$6.72	(68%)	142	(297)

Like so many other groups active in the Nash space, Madrigal saw its shares jump on a positive phase II trial. Mirati has been a steady riser all year thanks to combination trials of sitravatinib with Opdivo and monotherapy data delivered at Asco, which were sufficient to support a \$139m post-meeting share offering. Crispr Therapeutics looks like it has dodged a bullet over safety worries, having completed the first half of the year on a 150% rise.

As for the losers, Faron's lone clinical asset was Traumakine, so when that failed in acute respiratory distress syndrome it was not surprising to see the group's value haemorrhage. Faron has fallen to cash levels while investors wait for the company to advance its next project, the immuno-oncology asset Clevegen.

Edge Therapeutics was hit by the halt for futility of its phase III study of EG-1962 in adults with aneurysmal subarachnoid hemorrhage. This was also the fate of Protagonist with its ulcerative colitis project PTG-100.

Despite having promising data for varlilumab in combination with Opdivo at Asco, Celldex suffered from the epacadostat aftershocks that hit several companies working with established immuno-oncology agents ([Asco event analyser - A year of reset expectations, June 7, 2018](#)).

Aquinox was a late entrant to this rank, having just last week announced the failure of a phase III trial of rosiptor (AQX-1125) for the treatment of interstitial cystitis/bladder pain syndrome.

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