

Esmo 2022 movers - Kras backfires



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Inhibition of Kras dominated Esmo, though probably not in the way some had hoped.

Esmo [promised to be a conference whose most important topic was Kras](#), and this is how it turned out. However, investors were left bemoaning Amgen's move to push a Lumakras late-breaker into the meeting, an ultimately costly strategy that contributed to \$12bn of value being wiped from their company's market cap.

The jury is still out on how this affects Amgen's rival Mirati, but there was better news for several small biotechs, *Evaluate Vantage's* analysis of stock movers over the Esmo period finds. Relay and Deciphera have come out of Esmo as clear small-cap successes, and there were some big moves during the actual meeting, even if overall the losers outnumbered the winners.

To be fair, only part of the \$12.2bn in market cap lost by Amgen can be accounted for by [Lumakras's disappointment in the Codebreak-200 trial](#). Amgen also had to contend with [US approval of Bristol Myers Squibb's Tyk2 inhibitor Sotyktu](#); the psoriasis drug, greenlit with an unexpectedly clean label, will likely hit sales of Amgen's blockbuster Otezla.

This analysis calculates share price moves from the close before the titles of presentations and abstracts briefly appeared on Esmo's website on August 18, and yesterday, September 13, when the conference formally ended.

Selected Esmo 2022 risers*

Company	Share price gain	Comment
Relay Therapeutics	22%	See text
Deciphera	21%	See text
Regeneron	12%	Regeneron stakes its Lag3 claim
Clovis Oncology	9%	See text
Ayala	8%	Springworks aims to Defi expectations
Daiichi Sankyo	7%	Esmo 2022 preview
Springworks	6%	Springworks aims to Defi expectations
Mirati	5%	Mirati needs some colorectal cancer urgency
Roche	1%	Sanofi and Roche's duelling Serd duds

*Note: *share price change calculated from Aug 18 to Sep 13.*

Among the risers Relay stood out, with data on its FGFR2 inhibitor RLY-4008 being impressive enough to fuel a \$300m secondary; the stock had been up 60%, but the raise managed to wipe out a big chunk of the Esmo-driven gains.

An 88% overall response rate in the RLY-4008 dose selected to take forward in cholangiocarcinoma represented double that of what existing pan-FGFR inhibitors have shown, noted Dr Chiara Braconi of the University of Glasgow, who discussed the data at Esmo. RLY-4008's selectivity might explain why a different toxicity profile seems to be emerging.

Diarrhoea and hyperphosphataemia, the biggest problems with pan-FGFR agents, were seen at “clinically insignificant” levels with RLY-4008, though stomatitis and nail toxicities were more common. Still, the data are early, and Dr Braconi said open questions included ensuring that the trial’s population was not biased for good responders, and whether RLY-4008 can also keep secondary resistance mechanisms under control.

Relay will report full data from the trial next year – the phase 1 portion included other FGFR-driven tumour types – and have the pivotal cholangiocarcinoma cohort fully enrolled by the first half.

Regeneron reported promising melanoma data with its anti-Lag3 MAb fianlimab, but its 12% climb owed much to [positive results with high-dose Eylea](#). Concerns over the desmoid tumour market hit Springworks and Ayala, though both rose over the Esmo period, while Clovis got a lift from the Athena-Mono trial of Rubraca in first-line ovarian cancer maintenance showing further benefit across various subgroups.

Mirati was up 5%, though this belies a 4% fall yesterday on concerns that lack of an overall survival benefit, revealed in Lumakras’s Esmo presentation, might jeopardise the chances of Mirati’s adagrasib securing US approval without randomised data.

Deciphera is struggling to rebuild confidence after a [big setback with its marketed GI tumour drug Qinlock](#), and updates on two follow-on assets were well received. Most encouraging were phase 2 data on vimseltinib, a CSF1 receptor kinase inhibitor for tenosynovial giant cell tumours, a rare cancer of joint tissue.

ORR hit 53% in a cohort of patients with no prior targeted therapy, and 46% in those previously treated with Daiichi Sankyo’s Turalio, which also hits CSF1R. Turalio last year became the first drug to win approval for TGCT based on ORR of 38%, with no responses seen for control; it carries a boxed warning of potentially fatal liver injury.

Many fallers

Amgen’s \$12bn of lost valuation dwarfed all other Esmo fallers, of which there were many. Immunocore made the classic mistake of cherry-picking data for an IMC-F106C abstract that overpromised, and paid the price when its Esmo presentation disappointed accordingly.

Merck & Co also lost \$12bn, though this had more to do with ongoing questions over a possible bid for Seagen and less with the group’s own low-key meeting, which featured several clinical failures. Seagen itself fell 15% even though an Esmo update backed the potential of a Padcev plus Keytruda combo in bladder cancer.

Exelixis scored a presidential session slot with full presentation of the Cosmic-313 trial that largely confirmed

what was suspected when [the company topline the data in July](#): despite significantly extending progression-free survival, adding Cabometyx to Opdivo and Yervoy in first-line renal cancer means more toxicity.

The fact that Cosmic-313 met its primary endpoint of progression-free survival was pretty much where the good news ended. “Response rates we saw in both arms, as well as the complete response rates, fell short of what we in the RCC community had hoped for,” said Dr Sumanta Pal of City of Hope, who reviewed the study for Esmo.

Complete responses of 3% were seen in both arms, which tested Cabometyx, Opdivo and Yervoy versus Opdivo and Yervoy. Stifel analysts say this showed that adding Cabometyx did not produce deeper responses, possibly because Yervoy use had to be dialled back to rein in liver toxicity. Whether an overall survival benefit will emerge remains a crucial unknown – final OS analysis has yet to happen.

And it was a Kras setting that featured Esmo’s biggest share price loser: an update from a [phase 1/2 study](#) of Cardiff Oncology’s PLK1 inhibitor onvansertib in second-line Kras-mutated colorectal cancer did not look any better than the [earlier look at the Asco-GI meeting that disappointed investors](#).

Meanwhile, Gritstone climbed after presenting early molecular response data with its vaccine-based immunotherapies, Slate v1 and Slate-Kras, in combination with Opdivo and Yervoy in Kras-mutated solid tumours – but was a loser over the whole Esmo period.

Selected Esmo 2022 fallers*

Company	Share price fall	Comment
Cardiff Oncology	-28%	See text
Plus Therapeutics	-26%	Early data on rhenium-186 nanoliposome from Respect-GBM glioblastoma trial
Immunocore	-22%	Actual ORR with IMC-F106C is 23%, versus 38% cited in abstract
Zymeworks	-22%	Questions raised over how ZW49 is differentiated vs Enhertu
Adaptimmune	-17%	44% ORR with ADP-A2M4CD8 across various cancers
Immutep	-16%	Regeneron stakes its Lag3 claim
Seagen	-15%	Cohort K of EV-103 trial gives ORR of 45% for Padcev, vs 65% for Padcev + Keytruda
I-Mab Biopharma	-13%	Lemzoparlimab continues to disappoint
Exelixis	-11%	See text
Gritstone Bio	-10%	See text
Amgen	-9%	Double trouble for Lumakras
Incyte	-7%	Regeneron stakes its Lag3 claim
Merck & Co	-6%	The new liver cancer entrants line up
Immatics	-6%	Readacross from Immunocore's disappointment in Prame
Biontech	-4%	ORR in trial of BNT211 fell from 43% to 25%
Bristol Myers Squibb	-4%	Keytruda secures a renal cancer monopoly

Note: *share price change calculated from Aug 18 to Sep 13.

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