

BEFORE YOU INVEST • DRUG PROGRAM INVESTMENT LESSONS

WHEN \$2 BILLION BUYS YOU A SEAT – NOT CERTAINTY

Lessons from what patient data reveals about drug programs



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PIK3CA case study



\$2B+

Paid by Novartis in early 2026
for the mutant-selective PI3K α inhibitor

A RATIONAL DECISION?

PIK3CA-mutated tumors are a high unmet need. There is enough signal in clinical trials from competing products to warrant FDA approval. What's not to like?

PIK3CA is part of the same pathway as HER2, and trastuzumab is one of the most successful oncology drugs of all time. So the expectation is that the mutant-selective PI3K α inhibitor also will be, but will it?

WHAT THE PATIENT DATA REVEALED

Patient data uncovered that *PIK3CA*, in contrast to *HER2* is not a solo driver. Here are the complications:

- On top of gain-of-function *PIK3CA* mutations, in many tissues *PIK3CA* gene gets amplified, likely affecting the ORR in such patients.
- These amplifications are driven by a nearby gene, not *PIK3CA* itself. Meaning that a likely resistance mechanism is already in place.
- The enzymes synthesizing substrate for *PIK3CA* are often hyperactivated, likely affecting the therapeutic window.
- In contrast to *HER2*, *PIK3CA* mutated tumors are typically “supercharged” by other mutations affecting PI3K or MAPK pathways.

Gene amplification frequencies on chr.3q

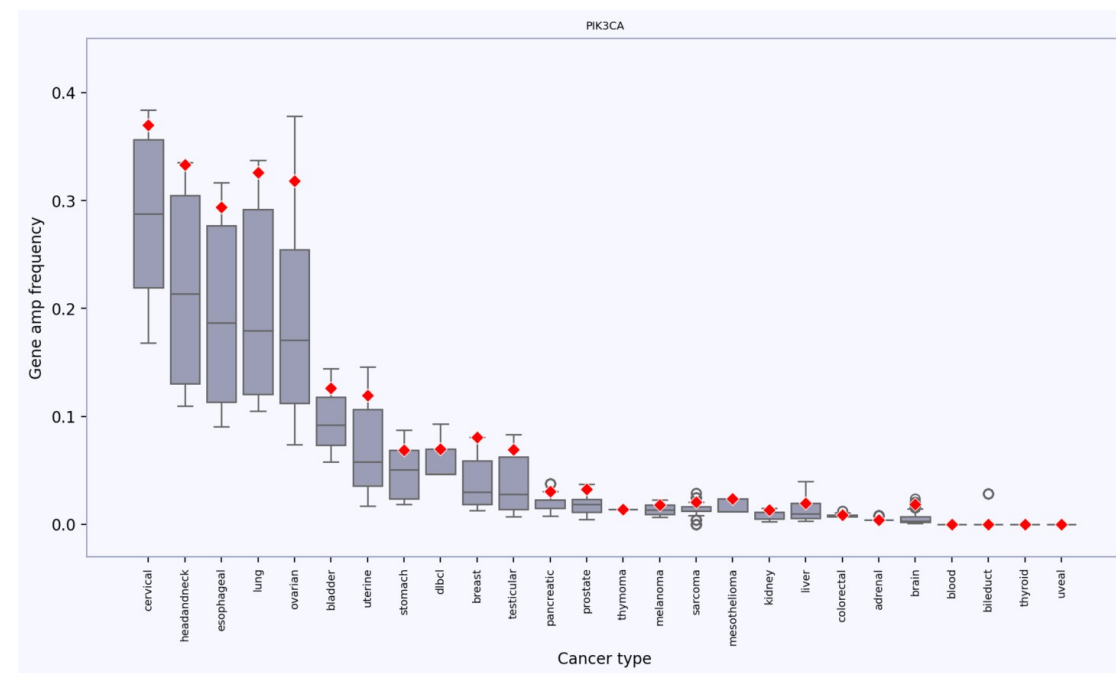


Figure 1. A box plot represents mean amplification frequency for all genes on chromosome 3q. Red diamond shows *PIK3CA* amplification frequency.

THE TAKE-HOME MESSAGE

IN THE PI3K α ARMS RACE, \$2 BILLION BUYS YOU A SEAT – **NOT CERTAINTY**



Patient data offers certainty

PIK3CA is not HER2, and the presence of the mutation is necessary but insufficient for spectacular success. Patient data could inform the clinical strategy.

Commercial opportunity

Yes, biomarkers narrow the addressable population, but pairing biomarker selection with combination therapy exploration increases the probability of success and can recover the lost market size.



STRATEGIC RECOMMENDATIONS

FROM INSIGHT TO ACTION

CONSULT PATIENT DATA FOR **RELIABLE OUTCOMES**

01 Clinical data have already proven that PIK3CA is not HER2

Ask the patient data why, and the path for PIK3CAi clinical and commercial success will emerge.

02 Solo vs team player.

Multiple mechanisms reducing the ORR were identified in patient data. Compare the effects of each and build a winning clinical strategy.

03 Patient data should be used before your trial begins.

There's a common misconception that clinical trials are required to assess response rates. Treatment-naïve patient data can actually identify factors that limit clinical response before any patients are dosed.





**Medicines intended to work in patients should
be developed with patient data in mind.**

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