

Before You Invest:

Lessons From What Patient Data
Reveals About Drug Programs



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When \$2 Billion Buys You a Seat -
Not Certainty



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?

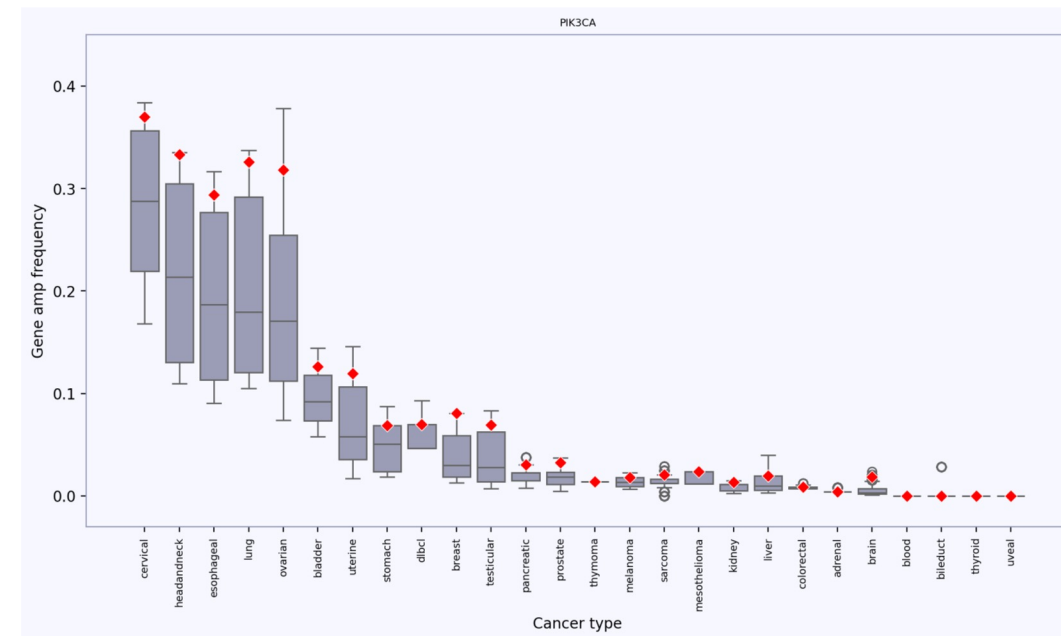
PIK3CA is part of the same pathway as HER2, and trastuzumab is one of the most successful oncology drugs of all time. So the expectation is that the mutant-selective PI3K α inhibitor also will be, but will it?

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



A box plot represent 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:

- ✓ **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.
- ✓ **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.
- ✓ **Patient data should be used before your trial begins.**
There's a common misconception that clinical trials are required to assess response rates. Treatment-naive 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.**

For inspirations check:

<https://www.gordion.bio/before-you-invest>