

Medical Treatments for Brain Tumors: *Looking towards the future*

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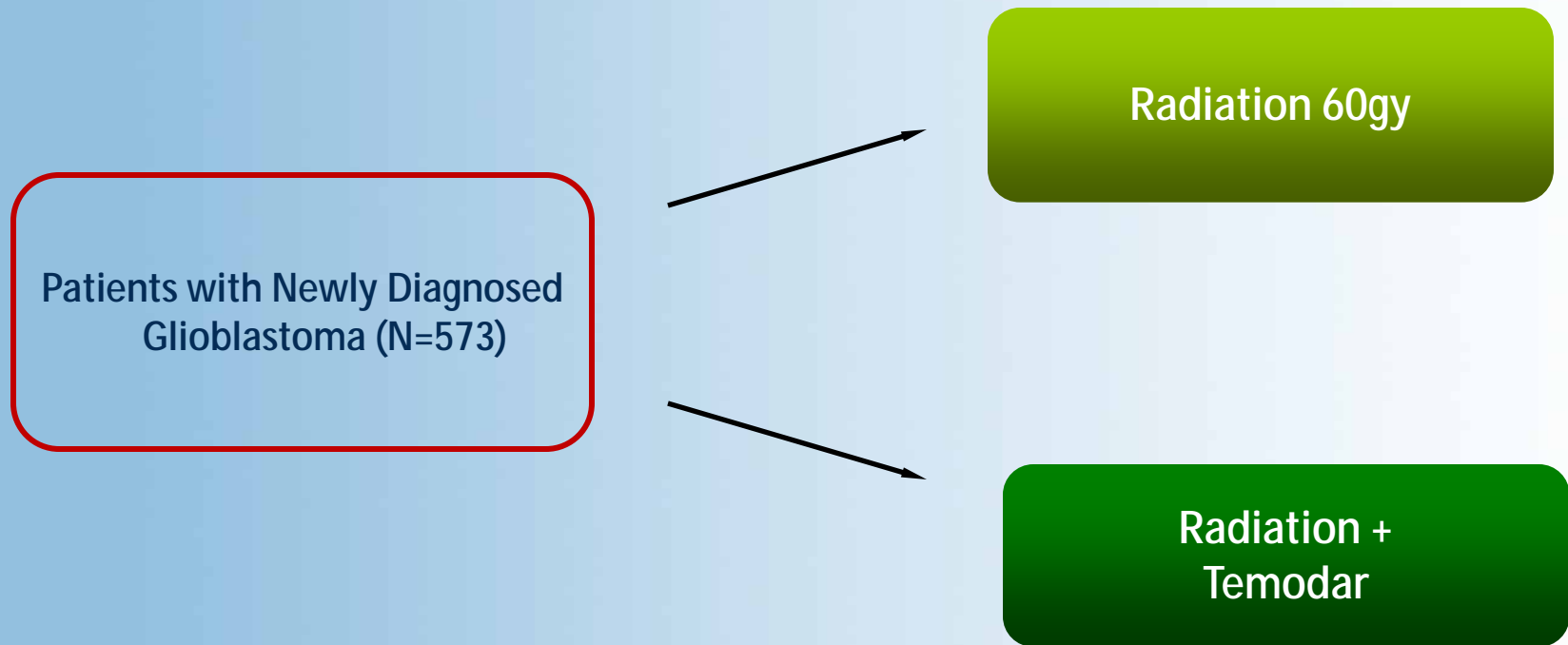
Developing better medical options for treating Glioblastoma

§ **Temodar: traditional chemotherapy**

§ **CPT-11: traditional chemotherapy**

§ **Avastin: anti-angiogenic (stops tumor blood vessel formation).**

radiation versus chemoradiation



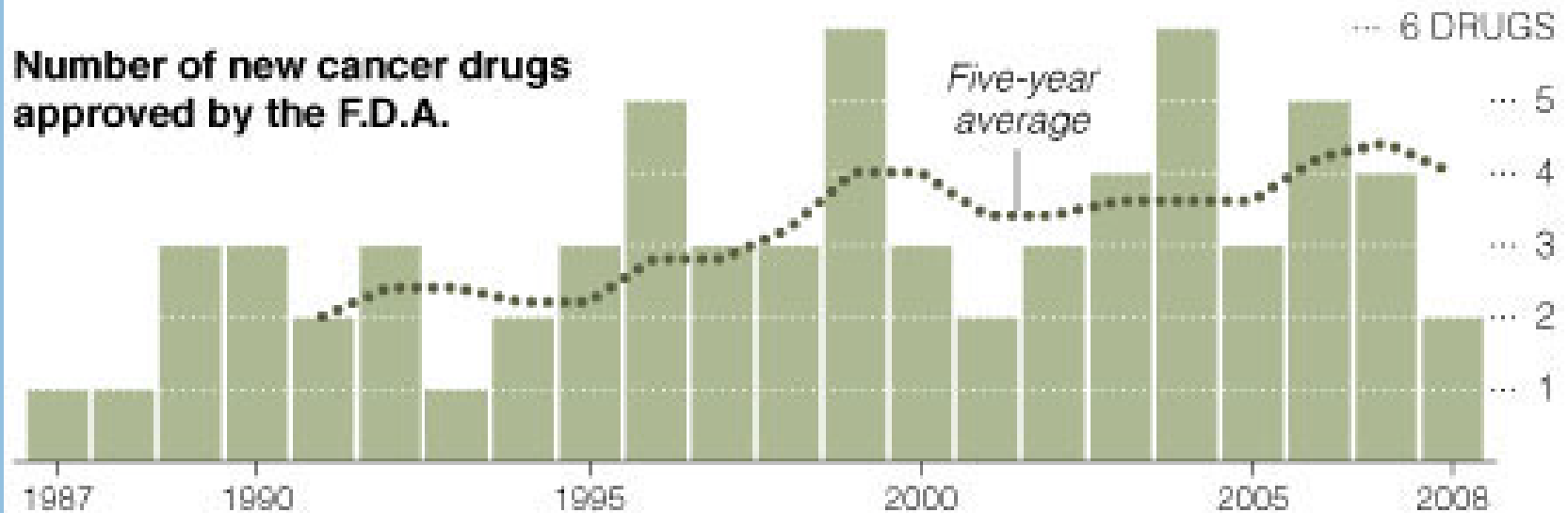
what is next?

**DEVELOP NEW DRUGS
& NEW STRATEGIES!**

Cancer Drug Approvals

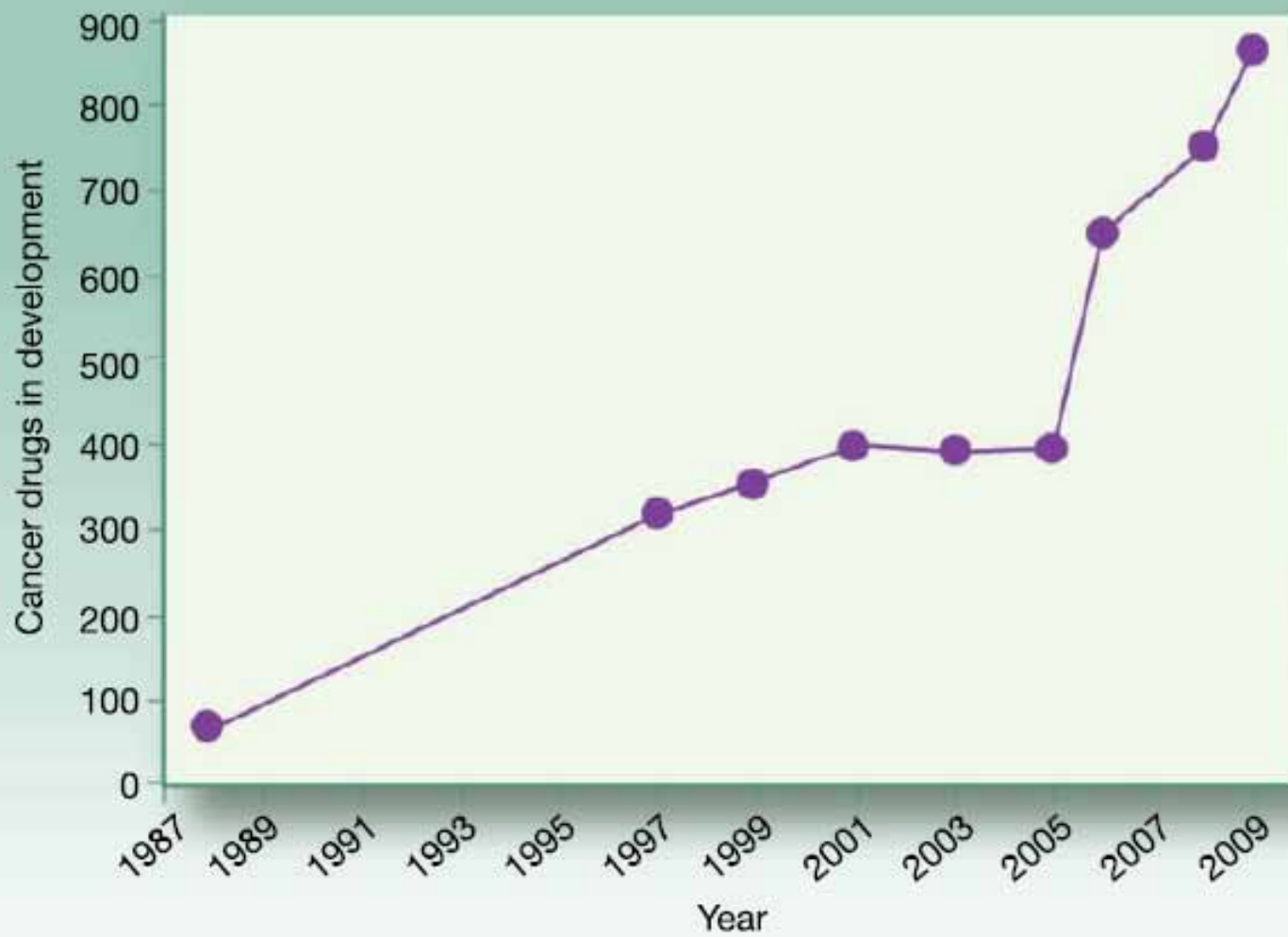
No cancer medicines can be sold without approval by the Food and Drug Administration. Federal law requires that the agency demand two "well controlled" trials before approving a drug; in cancer, the Food and Drug Administration is often satisfied with just one.

Number of new cancer drugs approved by the F.D.A.



Source: F.D.A.

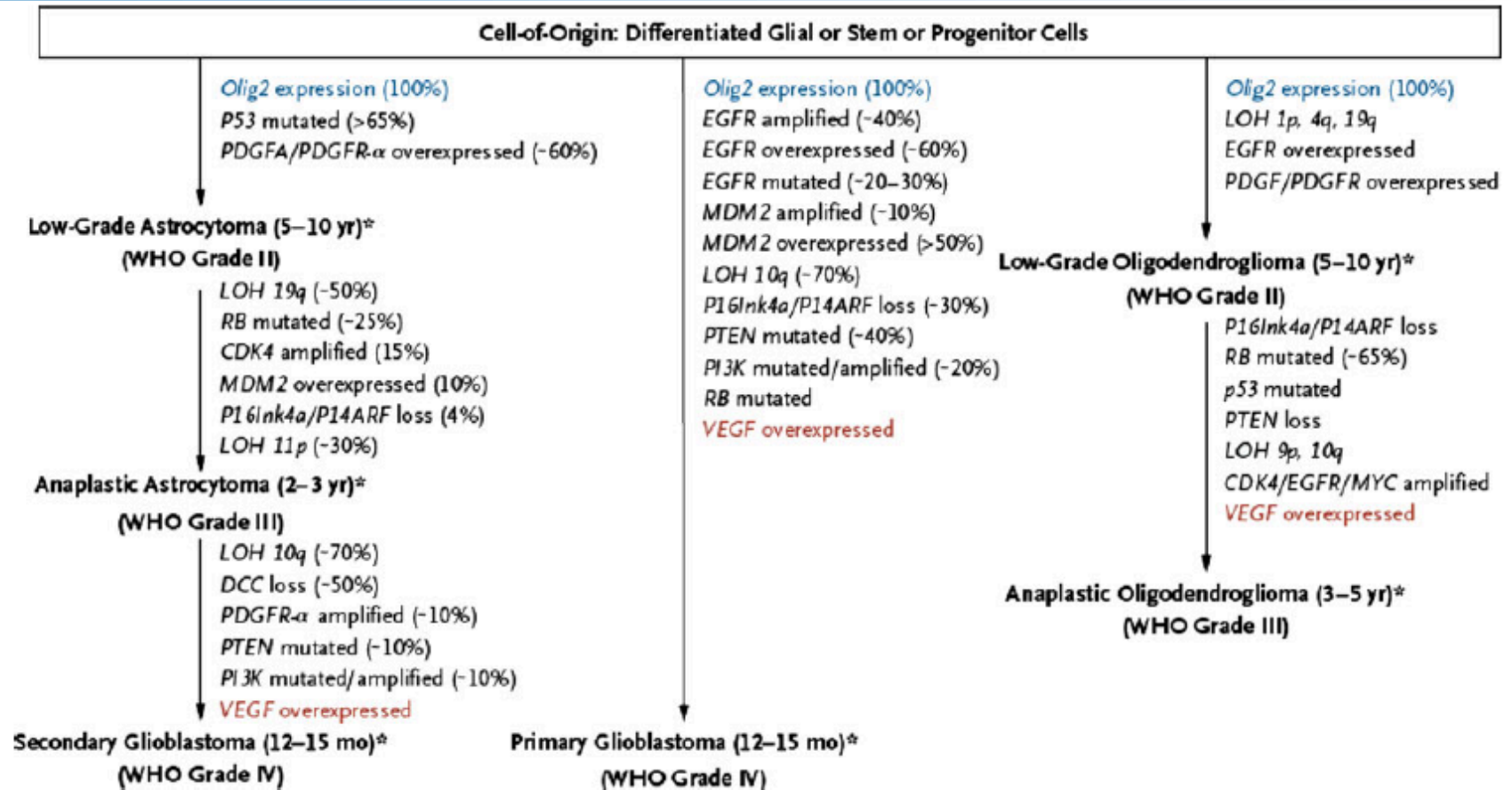
THE NEW YORK TIMES



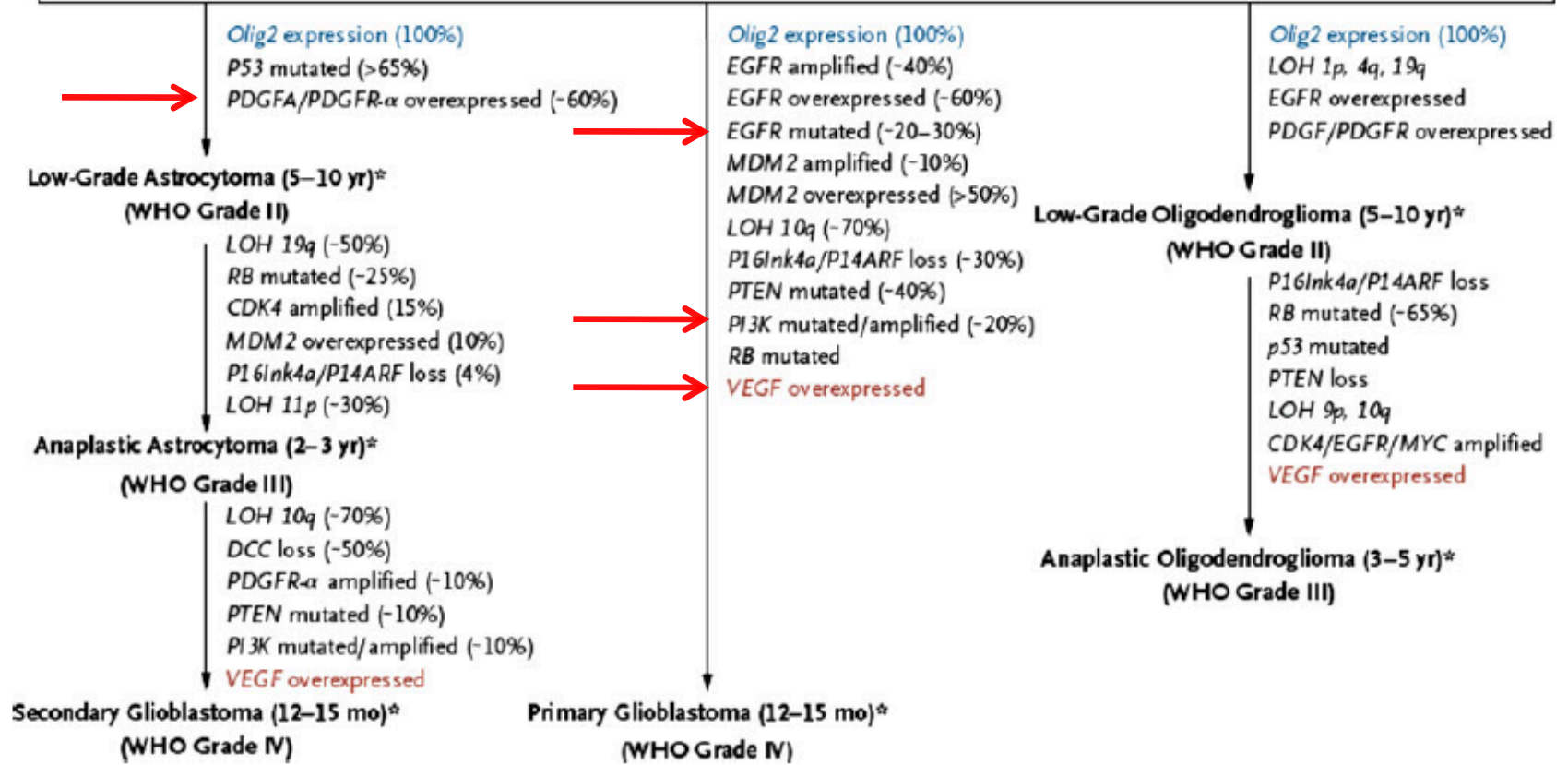
CCR Focus



Genetic alterations



Cell-of-Origin: Differentiated Glial or Stem or Progenitor Cells



UCBTC Portfolio Glioblastoma (GBM)

ANIMAL STUDIES

NOV-CTER
In vitro-In vivo
SISENE-UC-NCI

BXQ-350
Pre-IND
BEXION-UC

PRIMARY TREATMENT

RTOG 0837
CEDIRANIB
Phase 2

AXITINIB
Phase II
ISS

CDX 110
Phase III
Celdex

DCVax-Brain
Phase II
Northwest Biotech

RELAPSE / RECURRENCE

RTOG 0929
ABT-888
Phase 1/2

BEZ235/RAD001
Phase I-II
ISS

AMG 465
Phase I
Amgen

BXQ-350
Phase 1
IIS

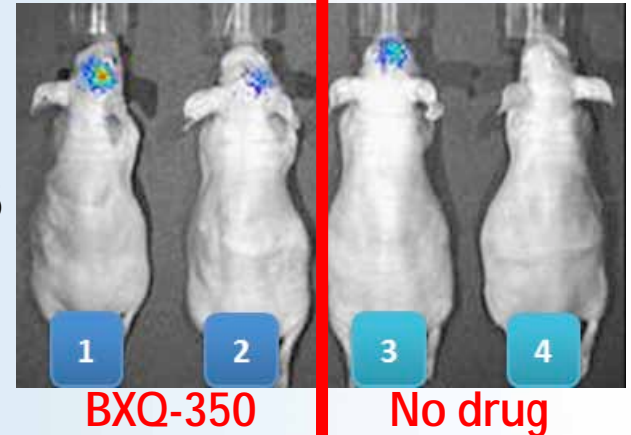
BXQ-350

BXQ-350: Anti-Cancer Nanovesicle Technology

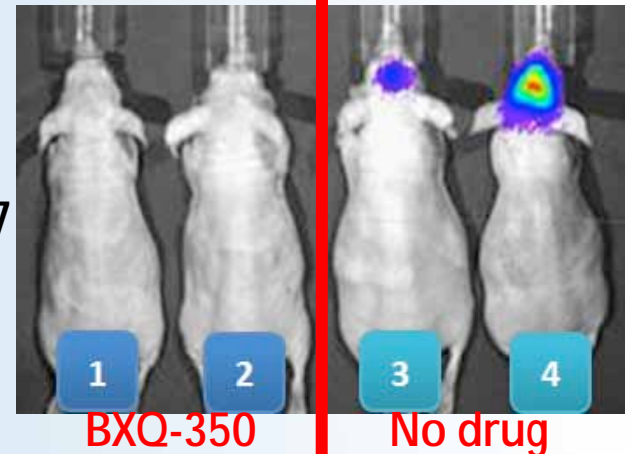
§ **BXQ-350 kills over 60 types of cancer cells in test tubes**

§ **BXQ-350 stopped the growth of human brain cancers with no adverse effects after 5 weeks of dosing in mice**

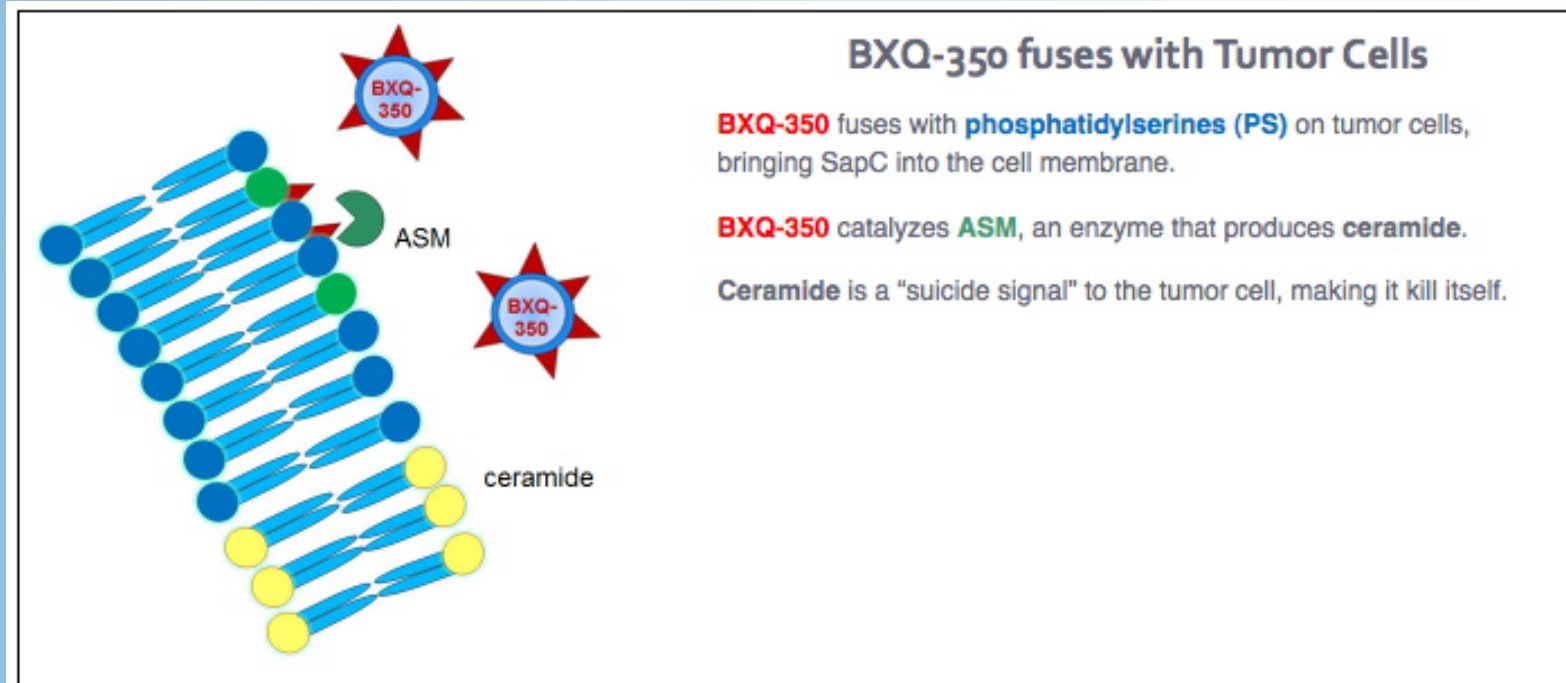
Day 5



Day 27



**BXQ-350 targets tumors and fuses to cell wall.
It kills tumors with a "suicide signal."**



BXQ-350

Phase I trial, first-in-human

§ **Timeframe:**

- Formulation (GMP): Q3 2011
- Animal toxicity study: Q4 2011
- Investigational New Drug application: Q1 2012
- IRB approval for use in patients: Q2 2012

coming soon
MARCH 2012!

**First human study in the world
conducted here in Cincinnati!**

Attacking Epidermal Growth Factor Receptor Variant III (EGFRvIII)

Elements of an Antibody-Drug Conjugate (ADC)

Antibody

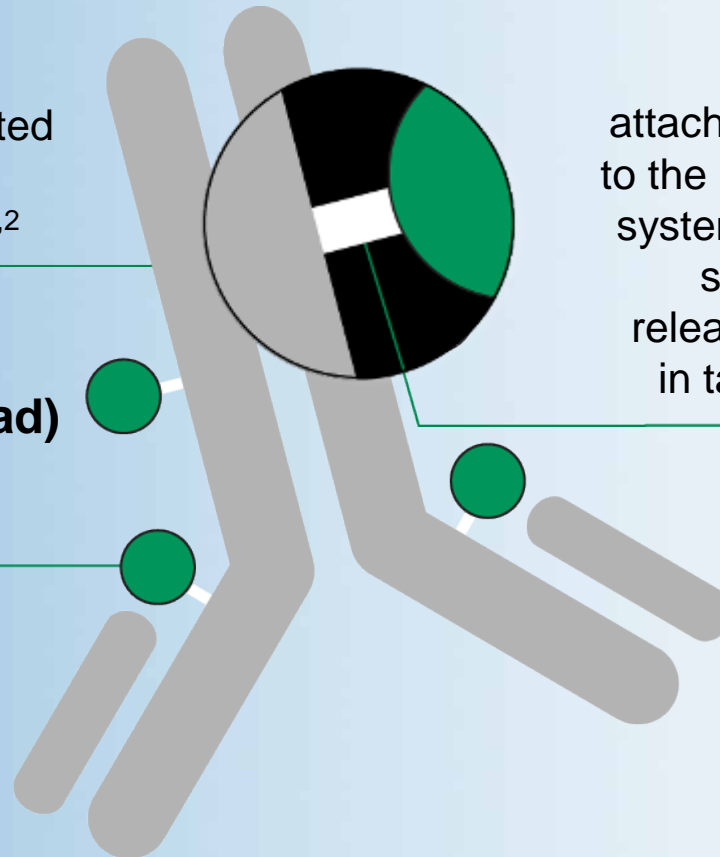
specific for a tumor-associated antigen that has restricted expression on normal cells^{1,2}

Cytotoxic agent (payload)

kills target cells when internalized and released^{1,2}

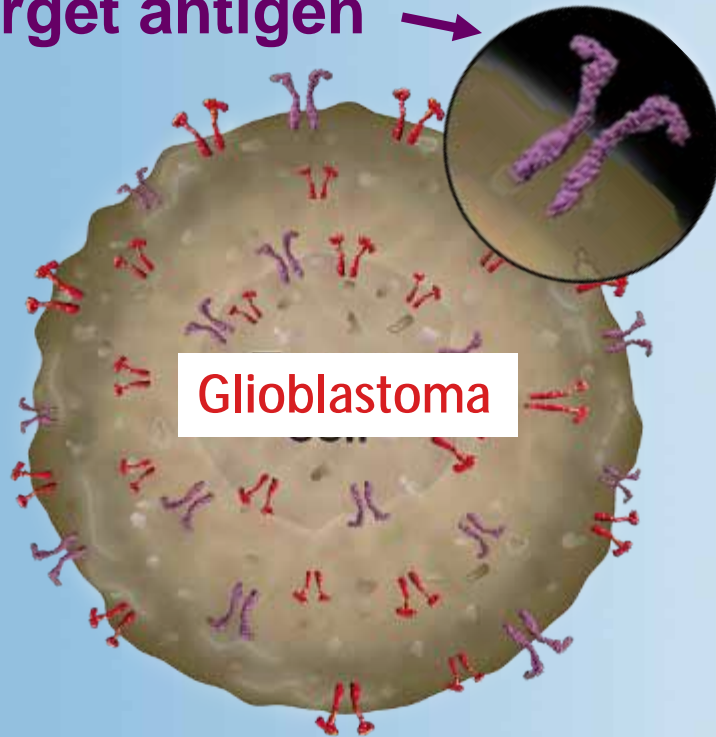
Linker

attaches the cytotoxic agent to the antibody. Newer linker systems are designed to be systemically stable and release the cytotoxic agent in targeted cancer cells¹⁻³



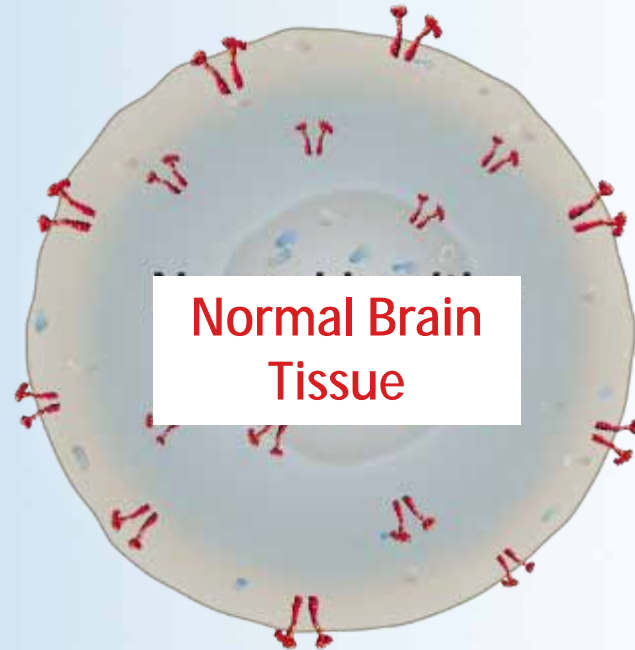
The Ideal Target Antigen is Differentially Expressed on Tumor Versus Normal Cells

Target antigen



Glioblastoma

Expressed abundantly
on tumor cells

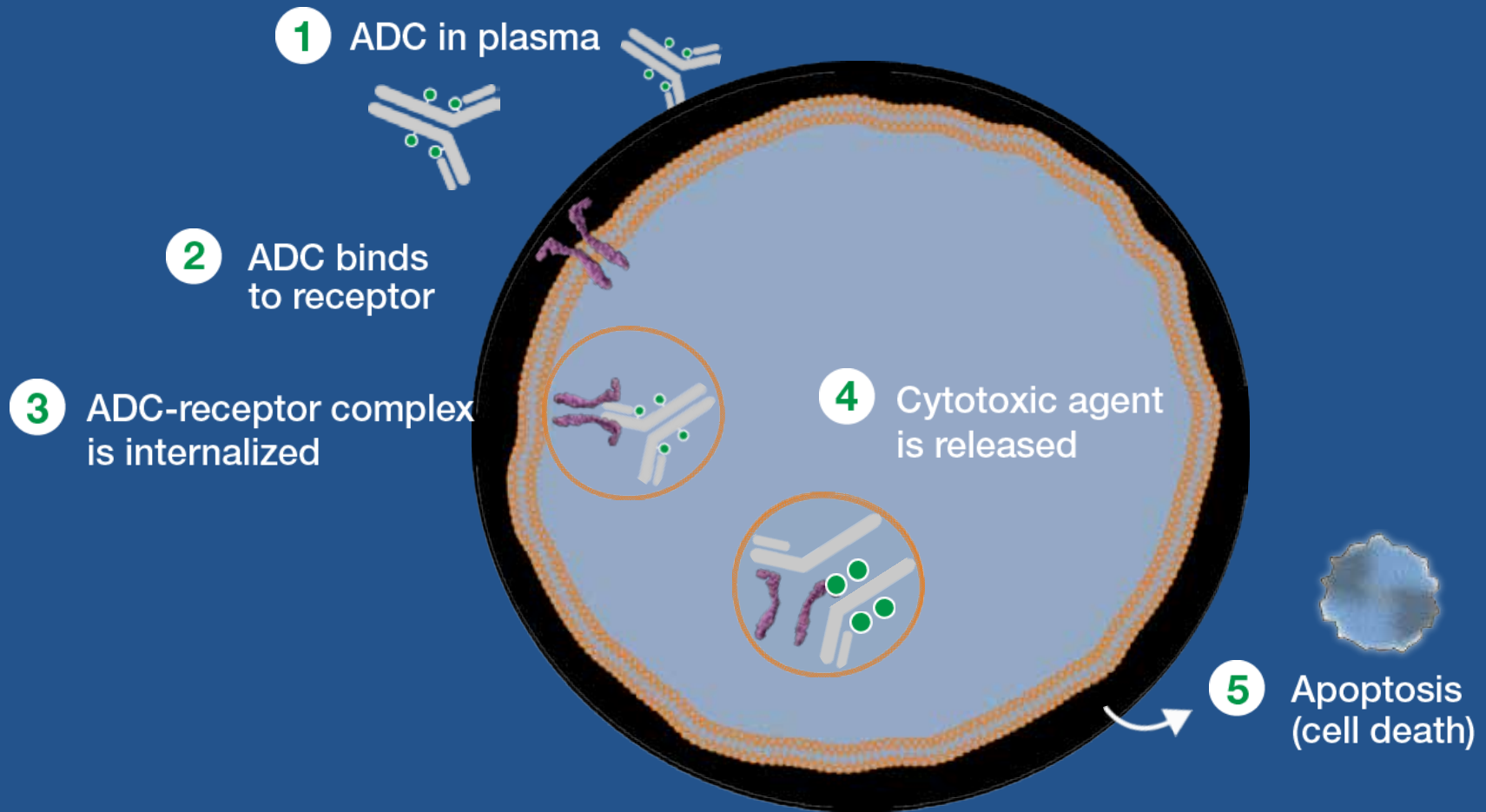


**Normal Brain
Tissue**

Limited or no expression on
normal or vital tissues

- Efficient internalization of target antigen increases drug delivery and enhances cell-killing

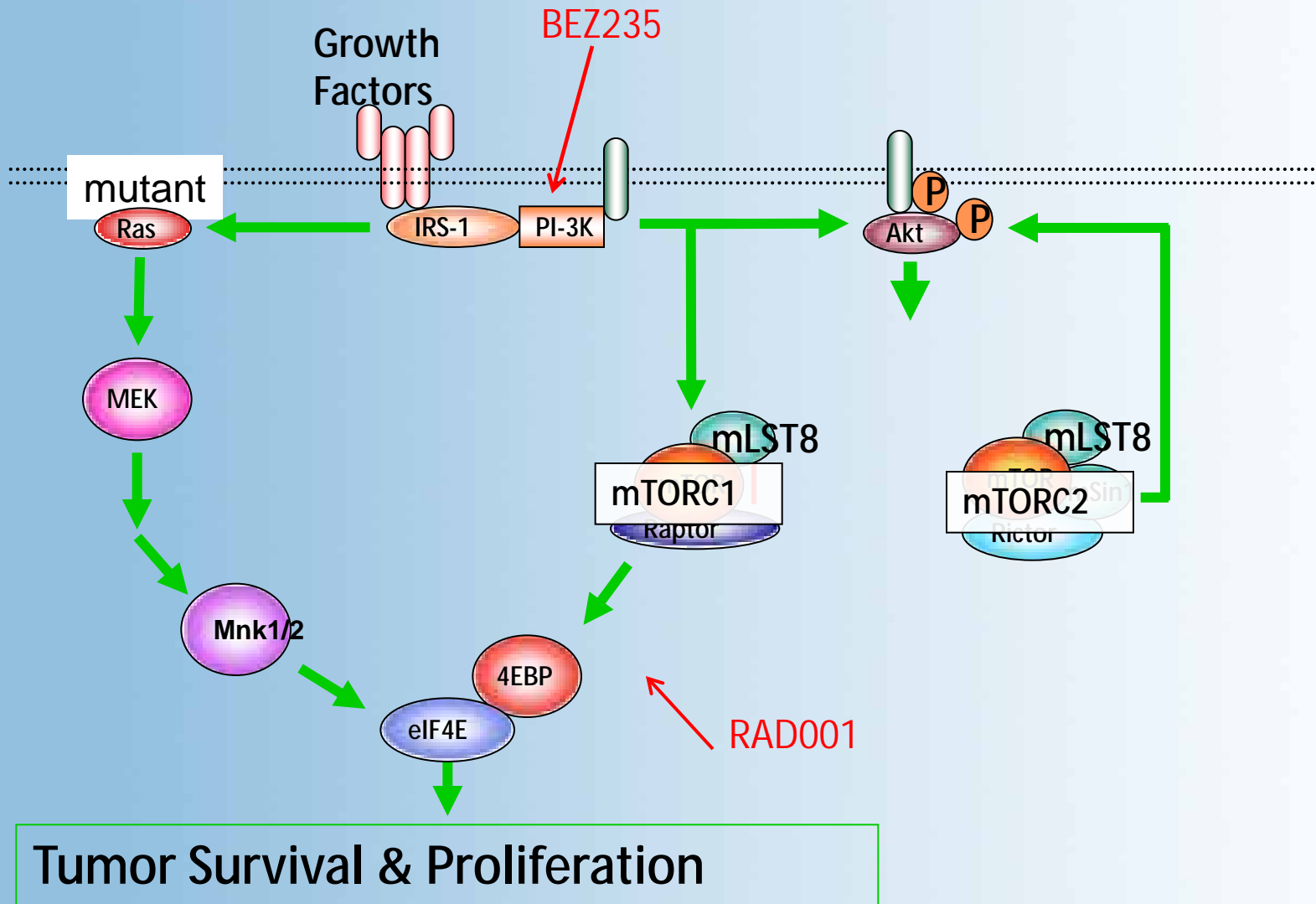
ADC Targeted Delivery of a Potent Cytotoxic Agent



NOVEMBER 2011!

Dual inhibition mTOR/PI3K

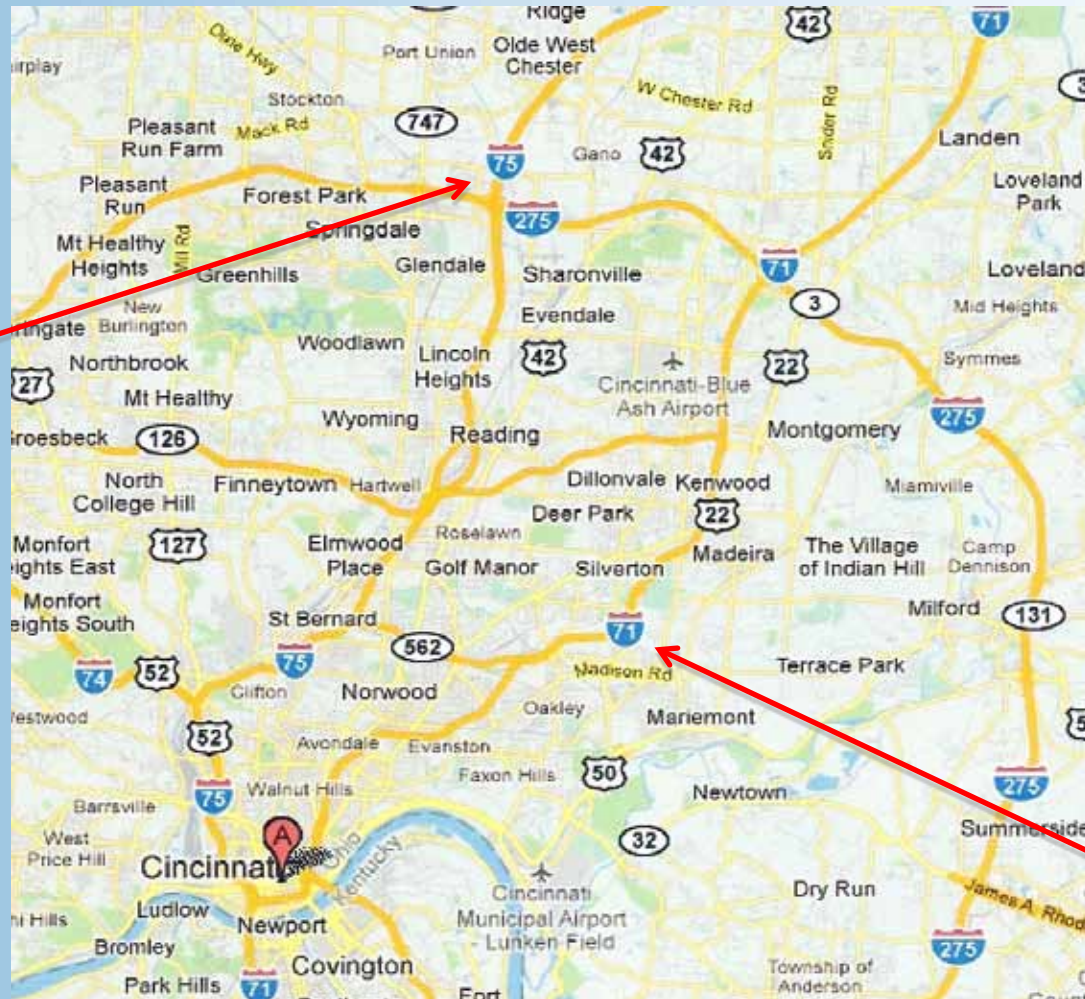
The Thomas's concept at UC from bench to phase 1



Dual inhibition mTOR/PI3K

Block delivery of food = starve the tumor

BEZ235

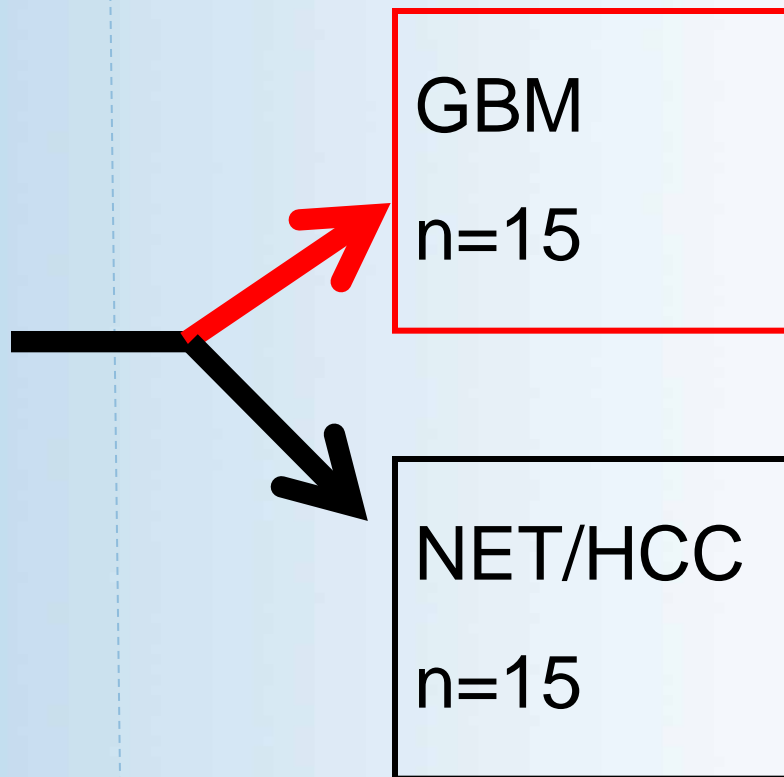


RAD001

PHASE 1B PORTION

PHASE 2 PORTION

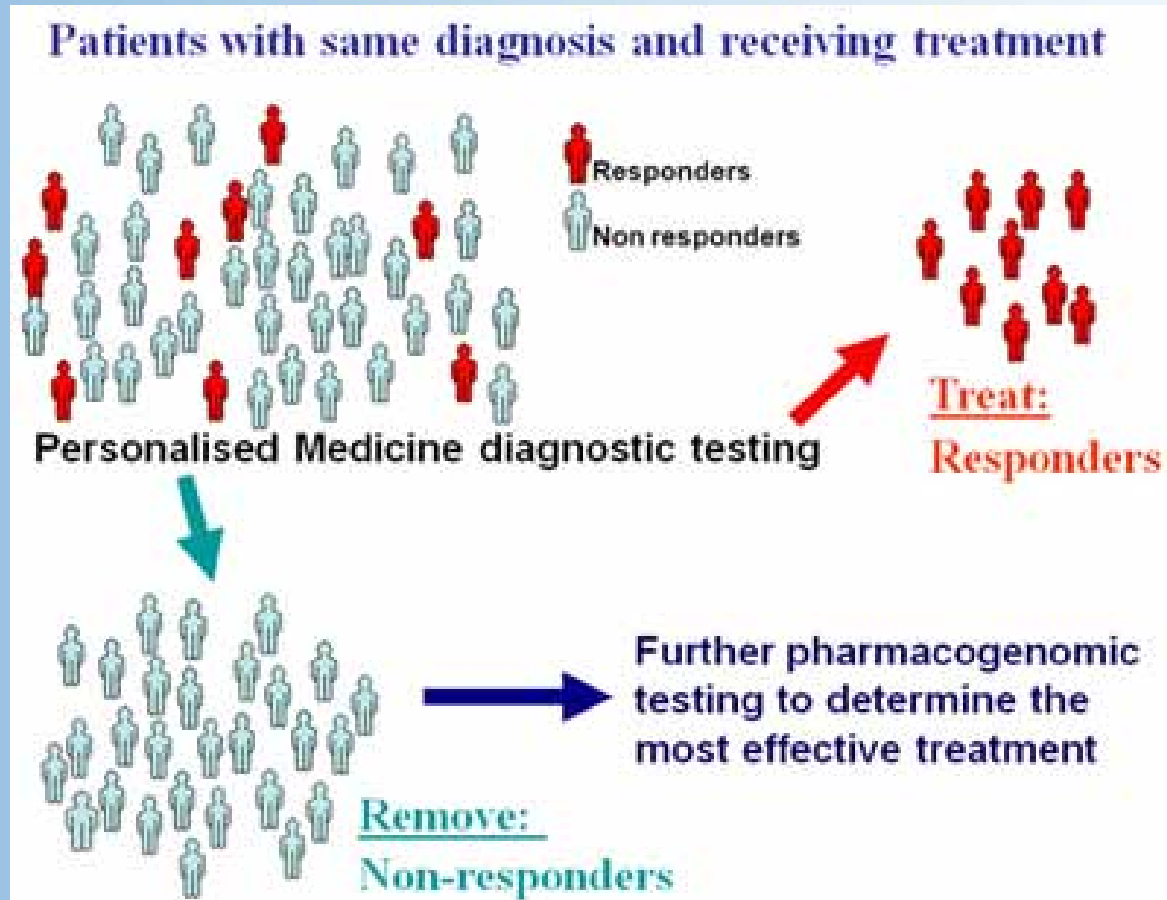
Dose Escalation
All Solid Tumors



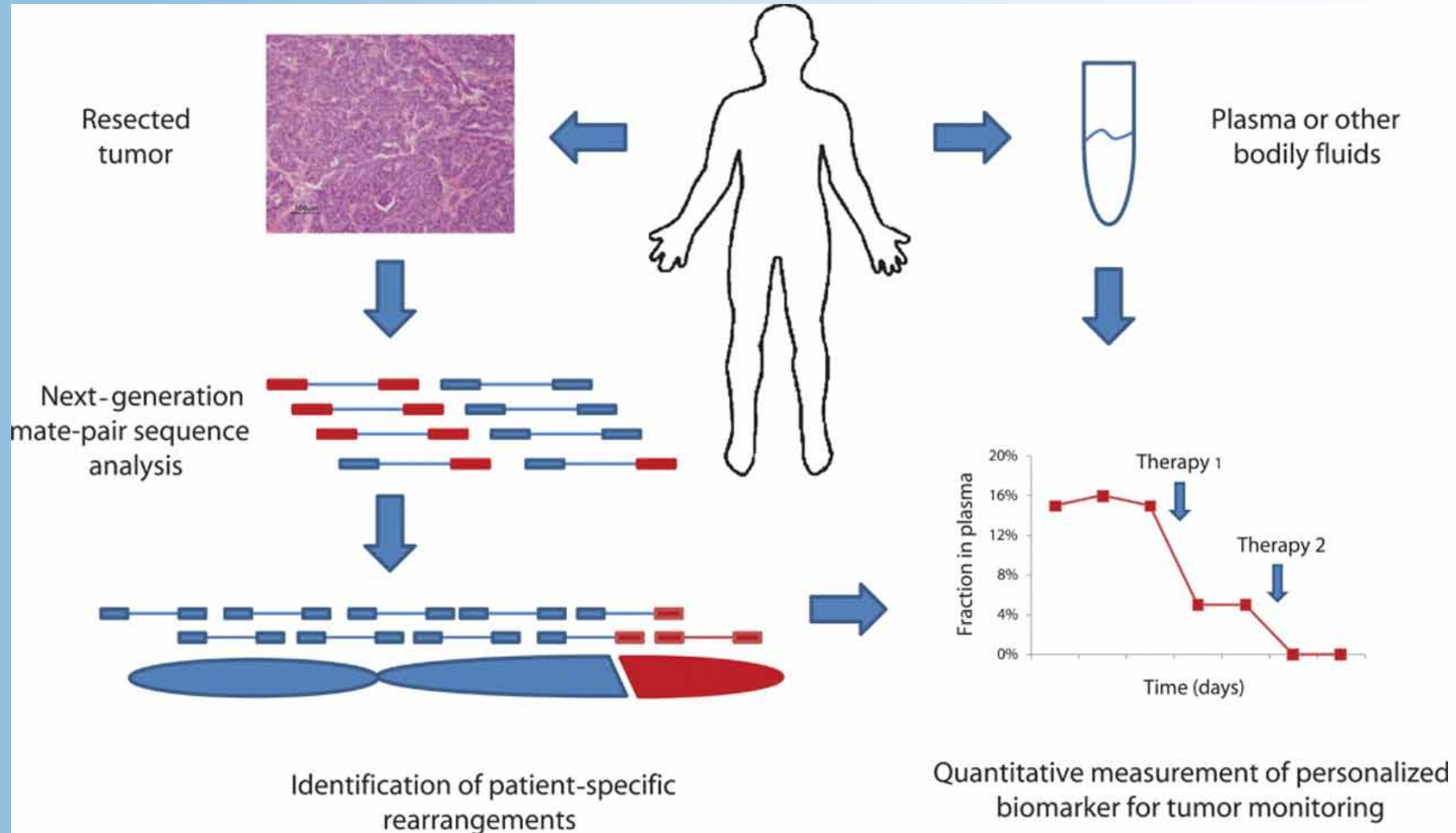
OCTOBER 2011!

Vaccine studies

Tailor-Made Therapy



Current study in GBM



Leary RJ et al, Science, 2010

