

Cautionary Statement Regarding Forward-Looking Statements



In order to utilise the 'Safe Harbor' provisions of the United States Private Securities Litigation Reform Act of 1995, AstraZeneca is providing the following cautionary statement. This presentation contains forward-looking statements with respect to the financial condition, results of operations and businesses of AstraZeneca. By their nature, forward-looking statements and forecasts involve risk and uncertainty because they relate to events and depend on circumstances that will occur in the future. There are a number of factors that could cause actual results and developments to differ materially from that expressed or implied by these forward-looking statements. These factors include, among other things, the loss or expiration of patents, marketing exclusivity or trade marks; exchange rate fluctuations; the risk that R&D will not yield new products that achieve commercial success; the impact of competition, price controls and price reductions; taxation risks; the risk of substantial product liability claims; the impact of any failure by third parties to supply materials or services; the risk of delay to new product launches; the difficulties of obtaining and maintaining governmental approvals for products; the risk of failure to observe ongoing regulatory oversight; the risk that new products do not perform as we expect; and the risk of environmental liabilities.

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Oncology and infection

Brent Vose

It's a changing world!



20th century

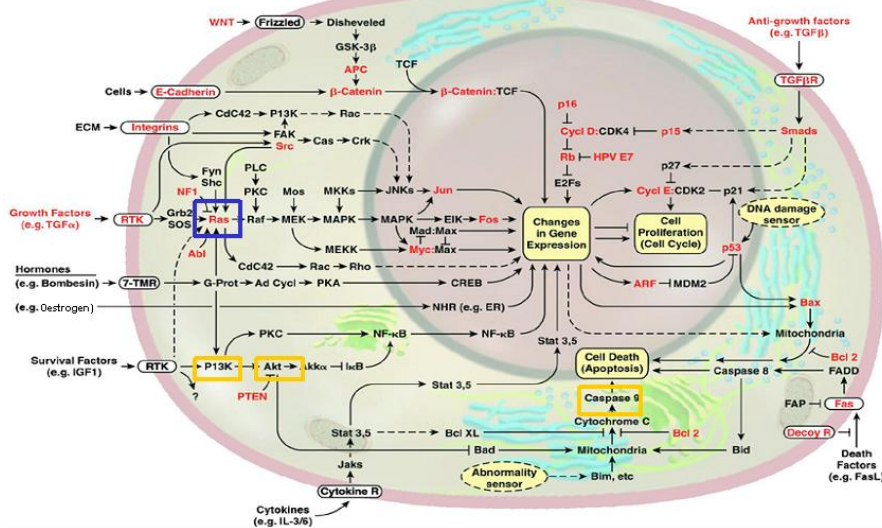
- Treat established disease
- Palliate incurable disease
- Diagnosis
 - Symptoms
 - Physical examination
 - Imaging
- Medical oncology
 - Cytotoxic chemotherapy
 - Intravenous
 - Toxic
 - Definition of correct disease
- Victory
 - Eradication of cancer
 - Cut it
 - Burn it
 - Poison it

21st century

- Prevent disease
- Treat early disease
- Diagnosis
 - Personal risk
 - Genomic/proteomic "exam"
 - Functional "targeted" imaging
- Targeted therapy
 - Oral
 - Biologic
 - Preventive
 - Definition of correct patient
- Victory
 - Prevent it
 - Eradicate it
 - Stabilise it

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Cancer: Complex science – lots of targets



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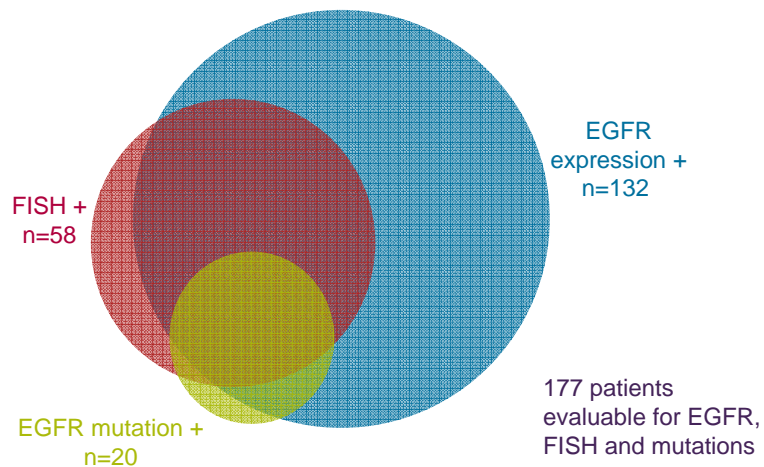
Pharmacodynamic biomarkers during development: Predictive efficacy



Question	Result
Does it hit the target in man ?	<u>Proof of Mechanism (PoM)</u> e.g. Enzyme inhibition, receptor blockade Go/No Go
Does it have an effect on the disease phenotype?	<u>Proof of Principle (PoP)</u> e.g. Increased cell death markers (apoptotic markers) Go/No Go
Does this result in a beneficial clinical effect?	<u>Proof of Concept (PoC)</u> e.g. Tumour size reduction Go/No Go

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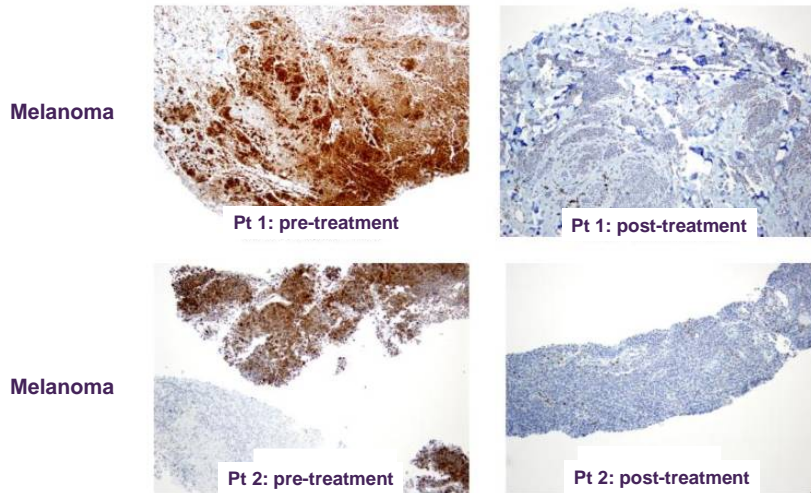
Identification of responding patients:



Key issue – how to get tissue from 80%+ of patients

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AZD6244: Excellent inhibition of MEK pathway at dose selected for phase II



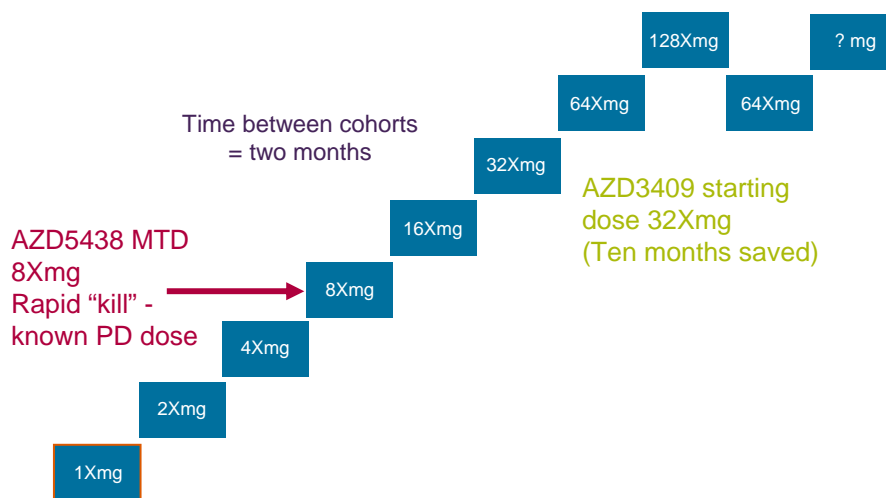
Data from Phase Ib: tumour tissues stained for pERK

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Example: Use of pharmacodynamic biomarkers for dose selection

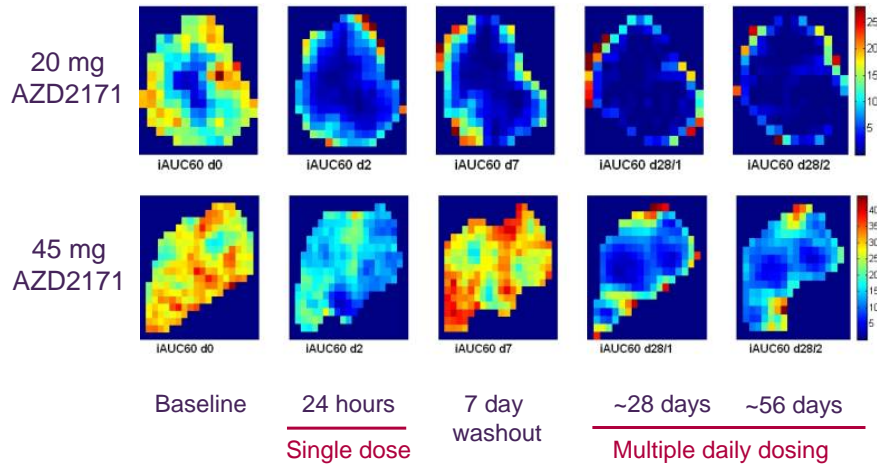


'Traditional' phase I dose-escalation trial



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DCE-MRI assessment of tumour blood flow and permeability

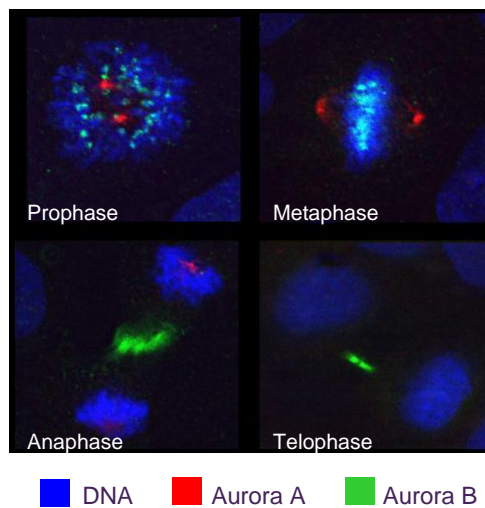


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Aurora kinases and cell cycle control

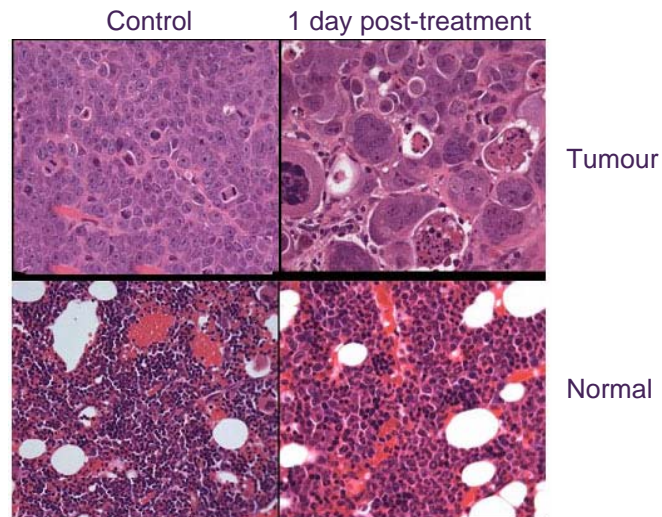


- Aurora kinases are mitotic regulators, which play a key role in chromosome segregation and cytokinesis
- Aurora A and B over-expressed in multiple tumour types offering therapeutic advantage
- AZD1152 blocks Aurora kinase B resulting in development of polyploidy and cell death
- Phase I ongoing



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Tissue changes following treatment with AZD1152: Tumour vs normal



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AZD0530 Selective Src/Abl kinase inhibitor



- Impressive biomarker data show activity in the clinical setting and allow dose setting for future trials
- Phase II trials in multiple settings will commence starting in 2H 2006
- CRADA in place with NCI to progress the further development
- Trials ongoing with NCI, NCIC and AZ

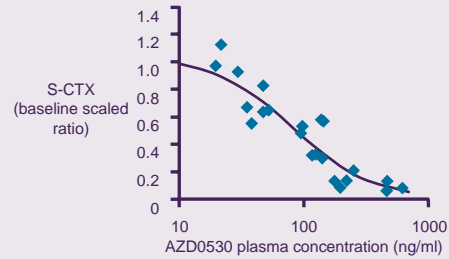
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Demonstration of activity of AZD0530 in man



Proof of mechanism

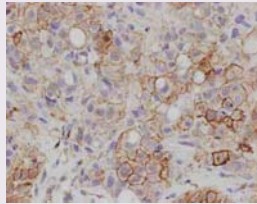
AZD0530 inhibits Src-regulated bone resorption markers in man at tolerated doses



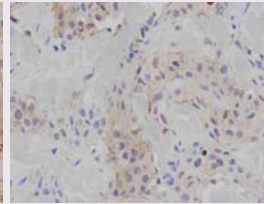
Towards proof of principle

Phase I biomarkers - AZD0530 inhibits FAK phosphorylation in human tumours at tolerated doses

Pre-dose



Post-dose



FAK pY861 – colorectal cancer abdominal metastasis

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AZD5180



- First antibody from Abgenix
- Wholly human antibody currently in preclinical development
- Anti-angiogenic in preclinical models
- Complementary with VEGF approach

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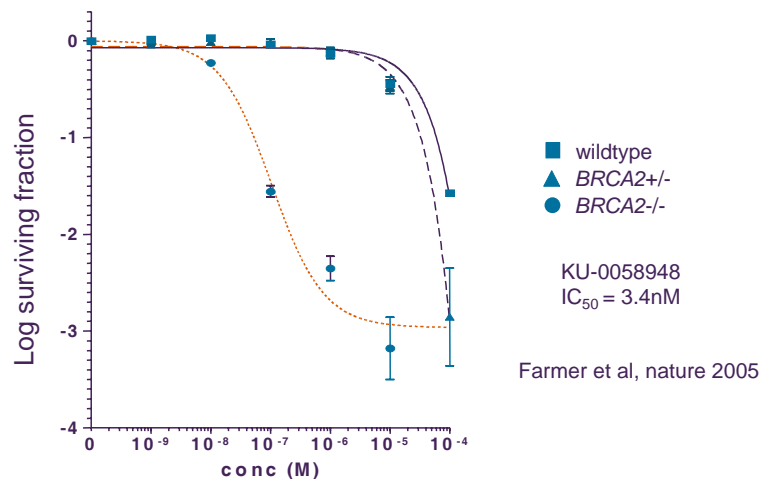
KuDOS acquisition



- Opportunity to access world-leading expertise in DNA repair (Professor Stephen Jackson, Cambridge)
- KU59436 (AZD2281), an oral poly-ADP-ribose polymerase (PARP) enzyme inhibitor, currently in phase I. Breast cancer studies start 2H 06
- Two other clinical development compounds – AQ4N (AZD1689) a topoisomerase inhibitor and Patrin™ – a DNA repair inhibitor (AZD5896) and two lead optimisation programmes delivering CDs within 12-18 months

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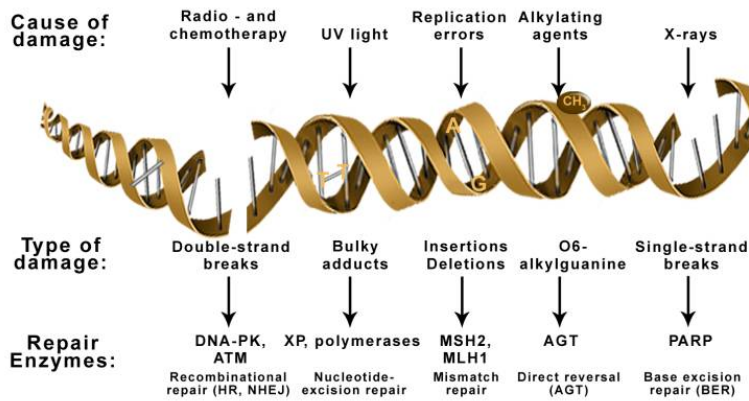
Brca2 -/- cells are very sensitive to PARP inhibition



~1000 fold differences in *BRCA2*^{-/-} v wildtype

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Types of DNA damage and repair

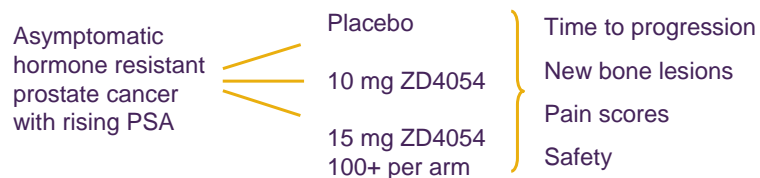


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ZD4054: Potential to be best in class



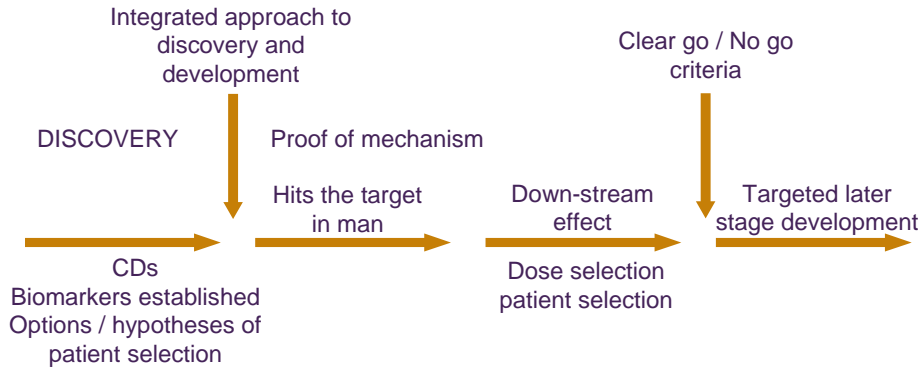
- Promotes apoptosis, decreased proliferation and effects on bone
- Minimally effective, biologically effective and maximum tolerated doses established in man



- Trial fully recruited with data in 3Q 06
- Clear go/no go criteria for immediate entry into Phase III

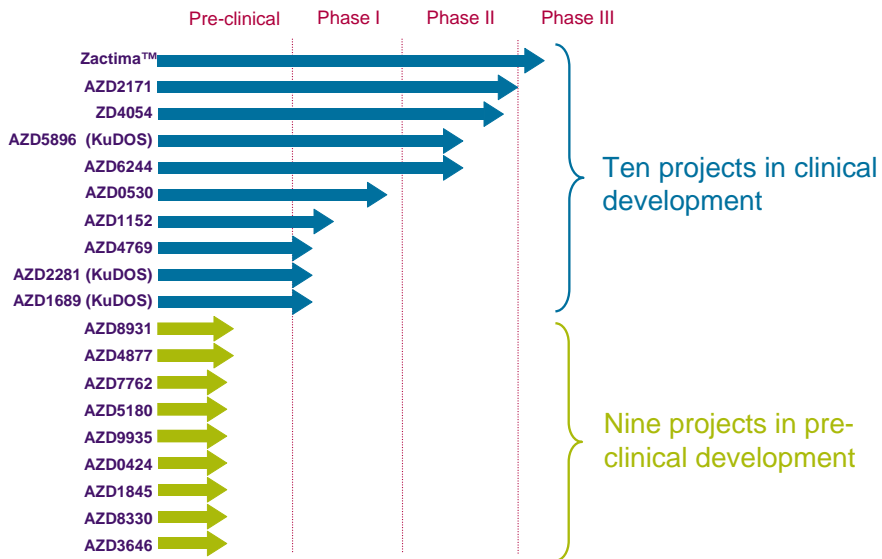
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Choosing the winners



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AZ Oncology portfolio (CDs – past nomination)



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