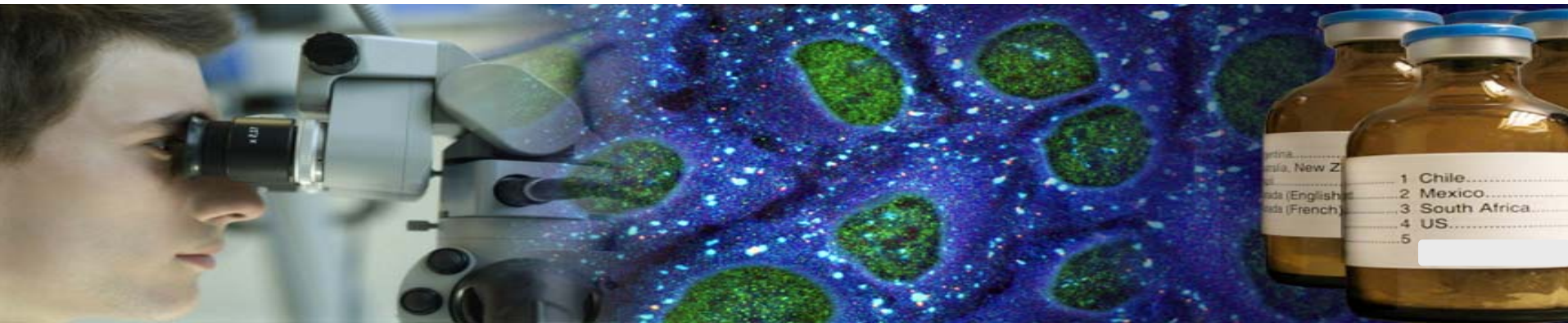


“The Future of NSCLC Therapy and the Re-Emergence of Hsp90 Inhibition”



NSCLC Expert Panel

March 25, 2011 • New York, NY

Forward-looking Statements

The following presentation may contain forward-looking statements about Synta Pharmaceuticals Corp. including, but not limited to, statements about the anticipated safety and efficacy of our drug candidates; the timing, developments and progress of our clinical and preclinical programs; our goals for registration-enabling trials; possible partnering and financing opportunities, reflect our current views with respect to future events and are based on assumptions and subject to risks and uncertainties that could cause actual results to differ materially from those expressed or implied by such forward-looking statements, including those described in "Risk Factors" of our Form 10-K for the year ended December 31, 2010 as filed with the Securities and Exchange Commission. Synta undertakes no obligation to publicly update forward-looking statements, whether because of new information, future events or otherwise, except as required by law.

Purpose

Ganetespib:

- 15 trials, >350 patients treated
- Good safety profile
- Clear single-agent clinical activity

→ What is the best path forward?

Panelists

Corey Langer, MD	Director, Thoracic Oncology; Abramson Cancer Center; Hospital of the University of Pennsylvania
Vincent Miller, MD	Attending Physician; Thoracic Oncology Service; Memorial Sloan-Kettering Cancer Center
Vojo Vukovic, MD	Chief Medical Officer, Synta
Suresh Ramalingam, MD	Assoc Prof., Dir. Div. Medical Oncology, Emory; Winship Cancer Institute PI Phase 1 trial of ganetespib + docetaxel; PI Phase 2b/3 trial of ganetespib + docetaxel in NSCLC
Eric Rowinsky, MD	Member, Board of Directors, Biogen-IDEC; Adj. Prof NYU; formerly: Chief Medical Officer, ImClone; Prof. Med. U.T. San Antonio; Assoc Prof. Johns Hopkins

Agenda

S. Bahcall, PhD

Introduction

Initial audience vote

C. Langer, MD

“Evolution of NSCLC Standard of Care”

V. Miller, MD

“Personalized Medicine in NSCLC; Role of Hsp90?”

V. Vukovic, MD

“Ganetespib in NSCLC”

S. Ramalingam, MD

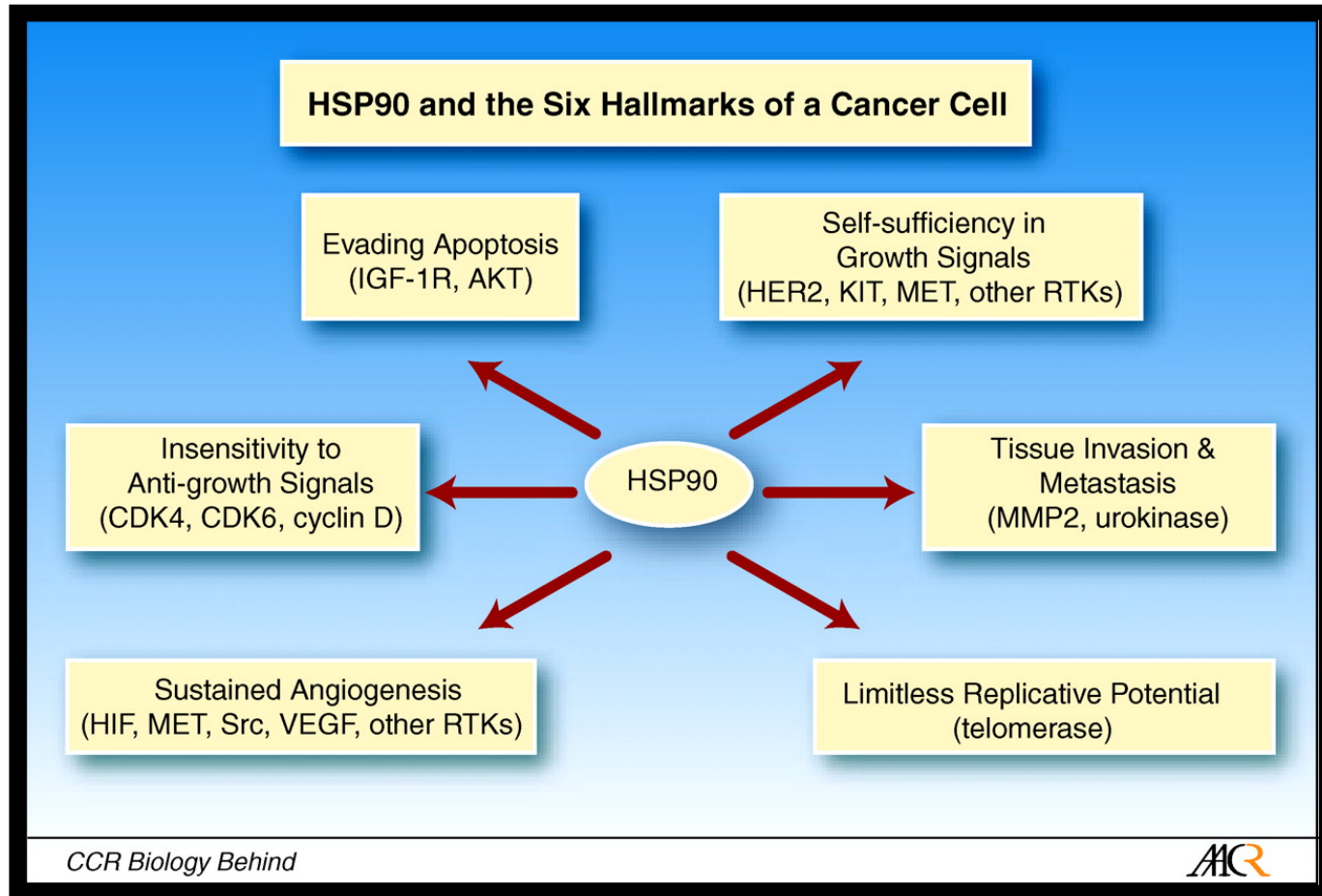
“Ganetespib and Docetaxel in Combination in NSCLC”

Discussion: Views on path forward for ganetespib and why
E. Rowinsky, MD ; C. Langer, MD

Final audience vote

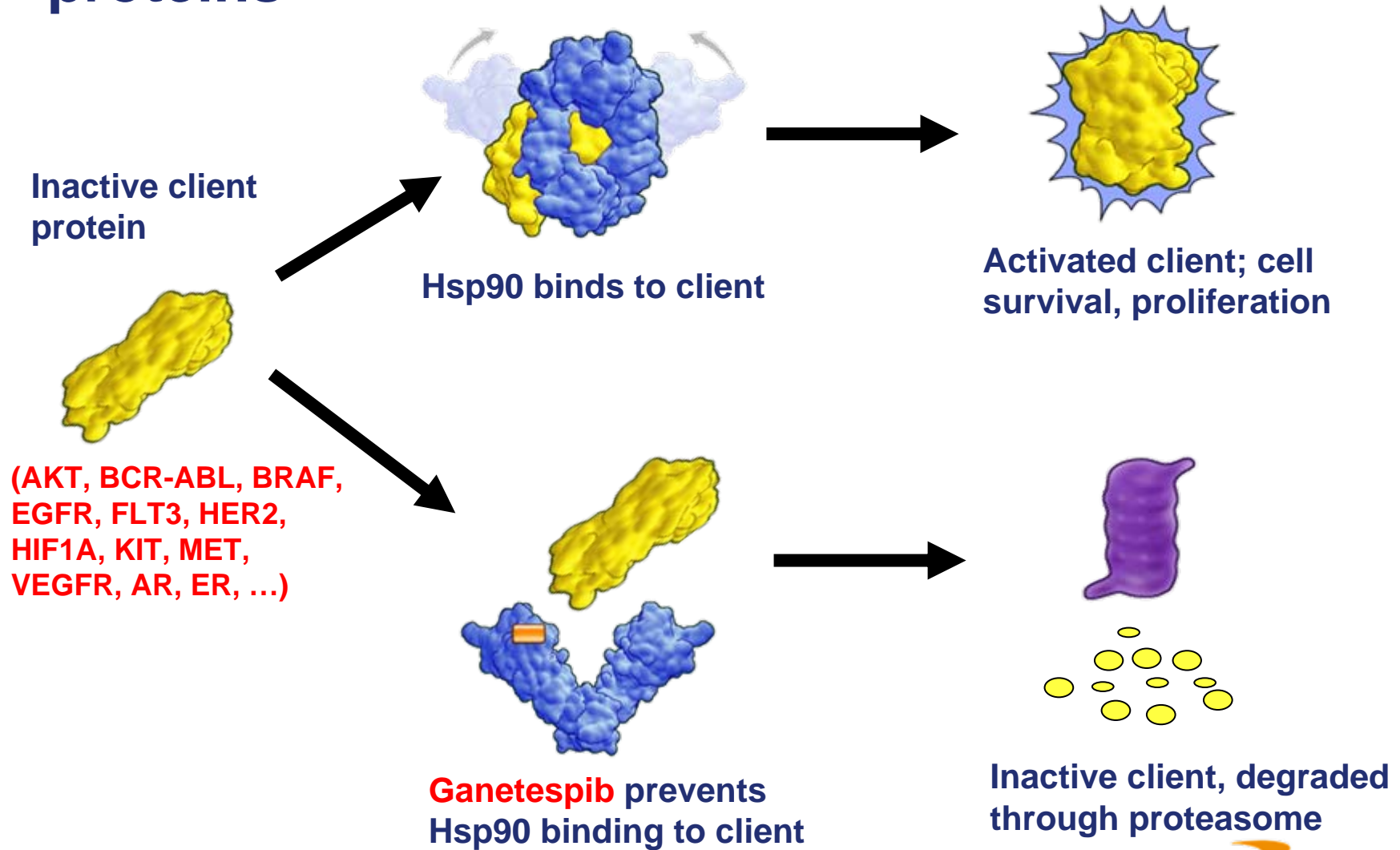
Q&A

Context: What is Hsp90?



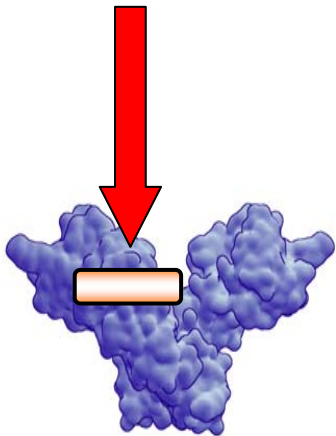
Xu, W. et al. Clin Cancer Res 2007;13:1625-1629

Inhibiting the chaperone degrades client proteins



Multiple validated targets

GANETESPIB



- ~~AKT~~
- ~~BCR-ABL~~
- ~~FLT3~~
- ~~RAS~~
- ~~c-MET~~
- ~~c-MET~~
- ~~c-Myc~~
- ~~EGFR~~
- ~~HER2~~
- ~~VEGFR~~
- ~~PDGFR~~
- ~~HER-1 α~~
- ~~CK4~~
- ~~ER AR~~

Gleevec

Erbitux

Tarceva

Sutent

Avastin

Herceptin

- Difficult to drug targets
- Multiple, complementary cancer-promoting pathways inhibited simultaneously

What's different with ganetespib?

Rationally designed:

1. Potency 10-100x improved over 17-AAG
2. Absence of liver, eye toxicities seen w other Hsp90i
3. Durable, objective tumor responses

Potency

Cancer Type	Cell Line	IC50 (nM)		Fold difference
		Ganetespiib	17-AAG	
ALCL	Karpas-299	10	452	45
AML	RS-4-11	8	1282	160
B Cell Leukemia	CCRF-SB	7	718	103
B Lymphoma	SU-DHL-4	20	2919	146
Breast	MDA-468	27	2484	92
CML	KU812	6	318	53
Colon	Caco-2	37	4946	134
Gastric	MKN-45	8	45	6
Gastrointestinal Stromal	GIST882	5	100	20
Kidney	ACHN	15	159	11
Large intestine	HCT-15	8	1800	225
Lung	NCI-H1838	14	278	20
Multiple Myeloma	RPMI-8226	28	73	3
Pancreas	HPAF	60	30	1
Pleura	MSTO-211H	7	246	35
Prostate	LnCap	17	266	16
Skin	A375	4	194	49
T Cell Leukemia	CCRF-HSB-2	2	273	137
Average				70x
Median				47x

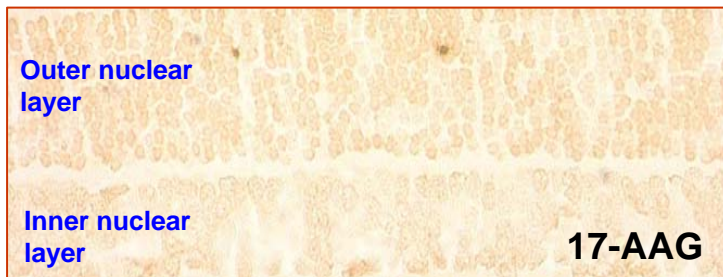
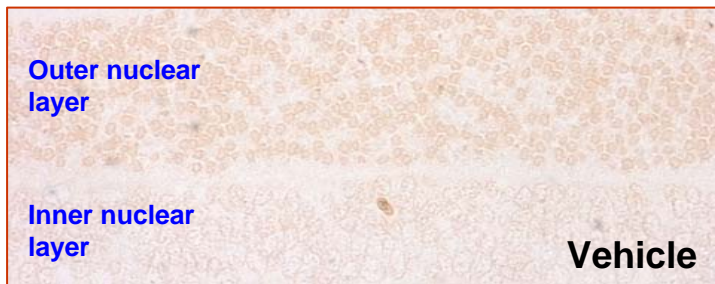
Eye toxicity

2nd-Gen Hsp90i	Clinically observed ocular toxicity (at MTD)
Ganetespib Synta	<3% (>200 mg/m² qw)
AUY-922 Novartis	89% (70 mg/m² qw)
AT13387 Astex	>50% (120 mg/m² biw)
SNX-5422 Pfizer	Terminated for excessive ocular tox

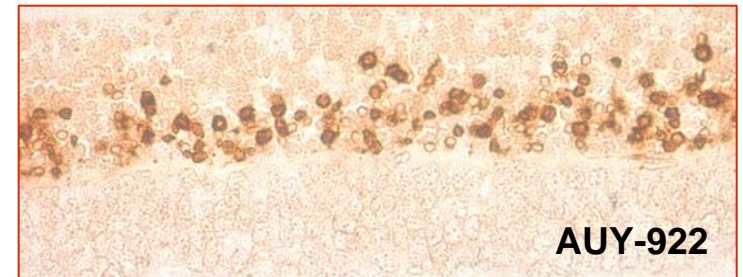
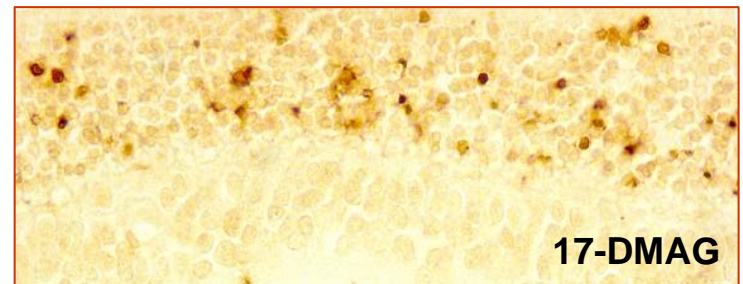
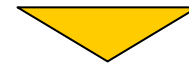
Source: ASCO Jun 2010; clinicaltrials.gov; Infante et. al., Pos # 375, AACR-EORTC Nov 2010

Retinal damage in preclinical models → clinical observations

Little/no eye toxicity in clinic



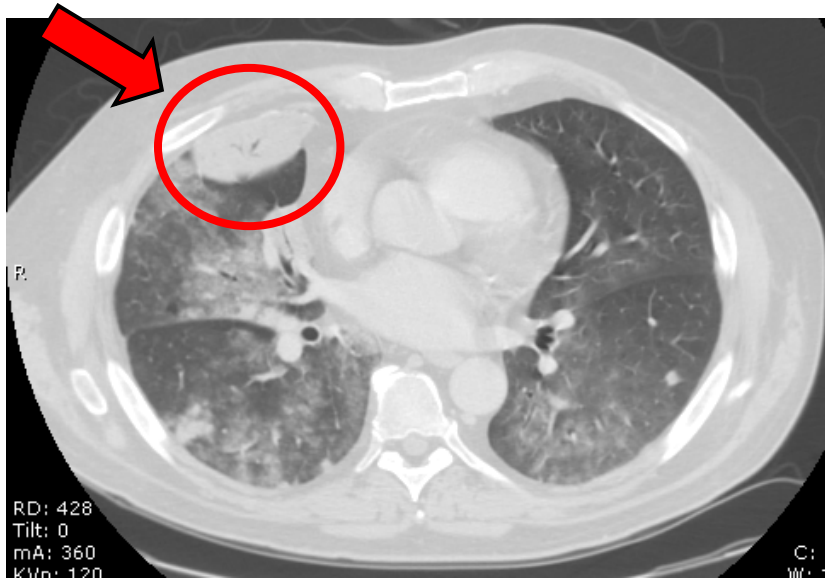
High incidence eye toxicity in clinic



Single-agent clinical activity

- Progressed on carboplatin, paclitaxel, Avastin, Tarceva, Alimta, topotecan, Velcade, retinoid; **duration: 2-4 months**
- **Ganetespib @ 150 mg/m² - monotherapy**

Baseline



After 4 cycles



- **Duration: 13 months**

Single-agent clinical activity

- Triple negative breast cancer, 39-year old woman
 - Adriamycin and Cytosan ; Taxol ; Xeloda + Avastin; Cisplatin ; Xeloda ; Cedarinib + Olaparib (pan-VEGFRi + HDACi) – PD
 - Ganetespib → PR
- NSCLC, 67-year old male
 - Carboplatin + Taxol + Avastin (3mo – PD) ; Sutent (1mo – PD)
 - Ganetespib → PR
- Other: Gleevec-resistant GIST, renal, melanoma, gastric

▶ Certain pts, highly refractory – showing pronounced, durable tumor shrinkage in response to single-agent ganetespib

What's different?

- ✓ Potency 10-100x improved over 17-AAG
- ✓ Absence of liver, eye toxicities seen w other Hsp90i
- ✓ Single-agent activity – durable, objective responses

Today's vote

Best path forward for ganetespib is

- a) Single-agent in highly-responsive subpopulations (“high Hsp90-addiction” cancers)
- b) Combination with docetaxel – Phase 2b/3
- c) Both in parallel
- d) None of the above – do more exploratory Ph 1/2 trials / other

Single-agent approach for ganetespib: different paradigm

Past 10
years:

Name of Drug → Name of the Patient

- Her2 inhibitor
- BCR-Abl inhibitor
- EGFR inhibitor
- BRAF inhibitor (V600E)
- EML4-ALK inhibitor

Hsp90 is different, because it is chaperone, not oncoprotein

Oncoprotein

One question

- How addicted is tumor to oncoprotein?

Chaperone

Two questions

- How addicted is tumor to oncoprotein?
- **How addicted is oncoprotein to Hsp90?**

>200 Hsp90 client proteins – but not all client proteins are created equal

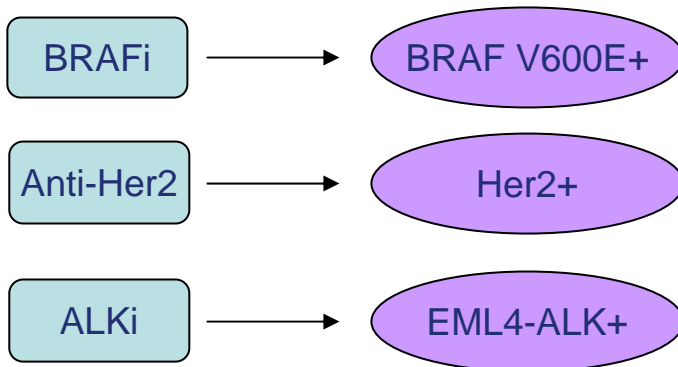
Hsp90-Addiction



Different paradigm

Targeting
Oncoprotein

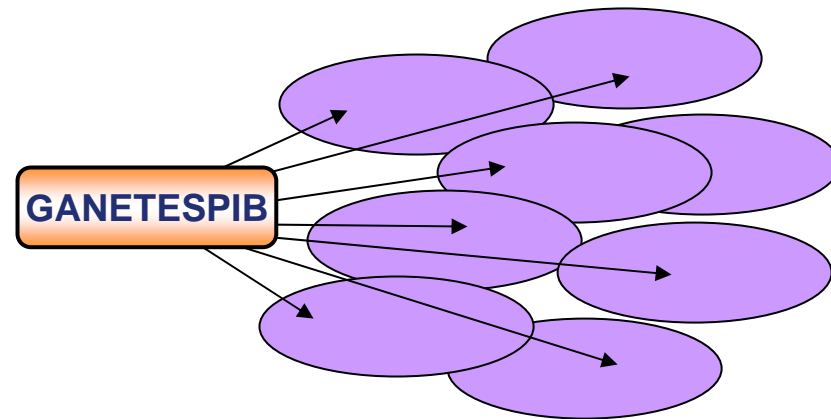
Unique high-response gene
profile



1 → 1

Targeting
Chaperone

Multiple high-response
gene profiles



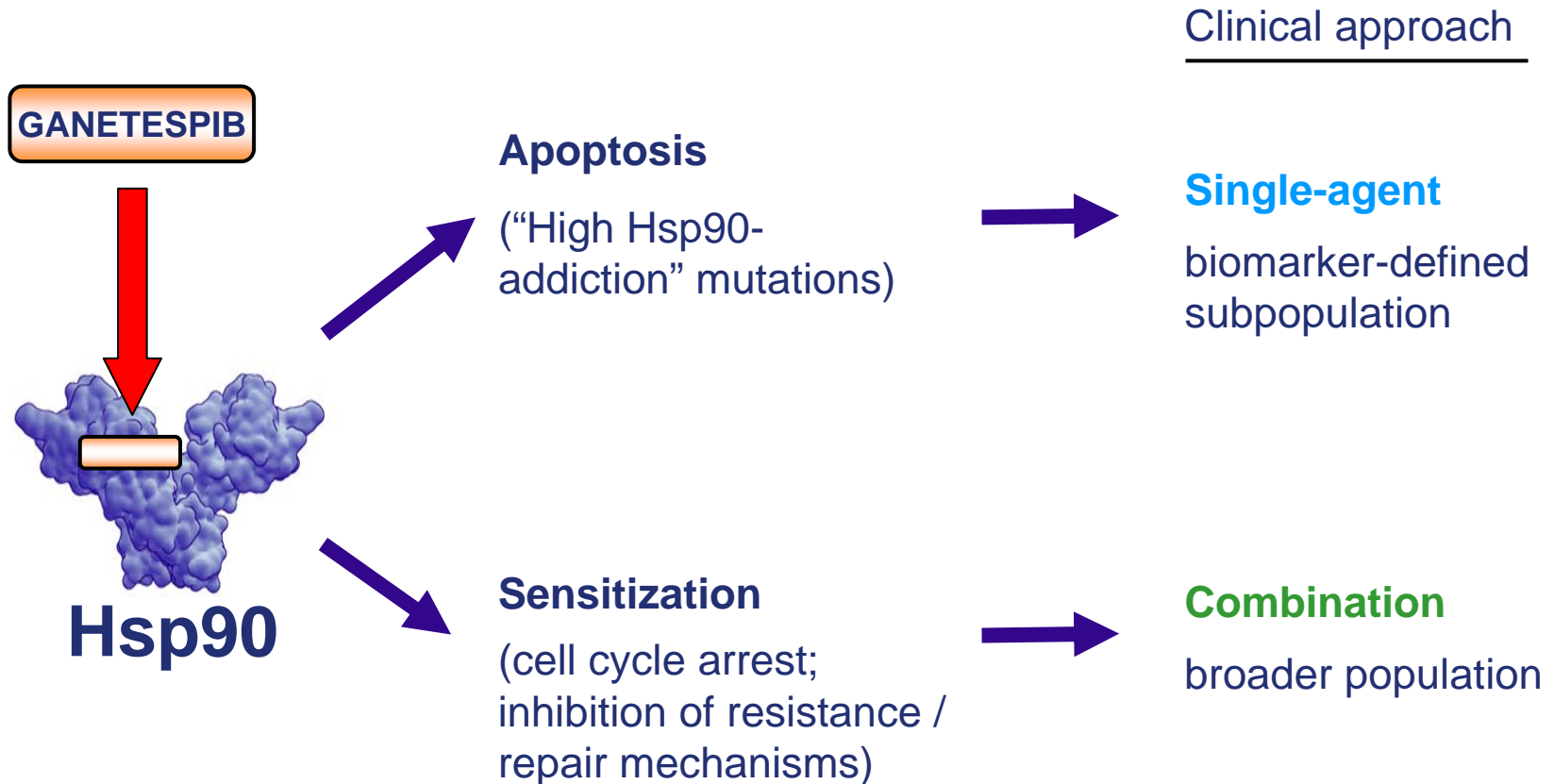
1 → Many

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Two effects of Hsp90 inhibition

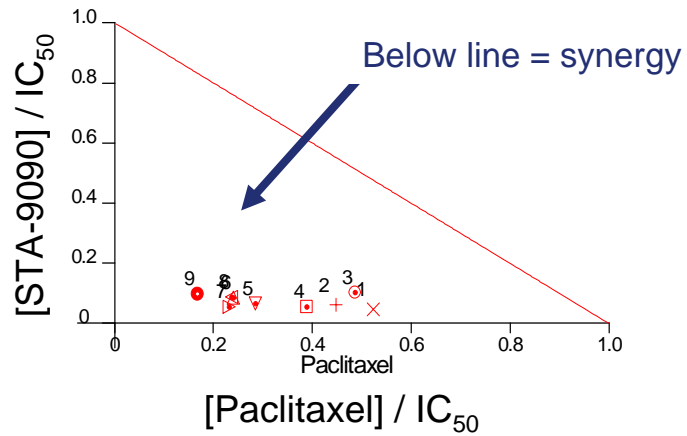


Combinations

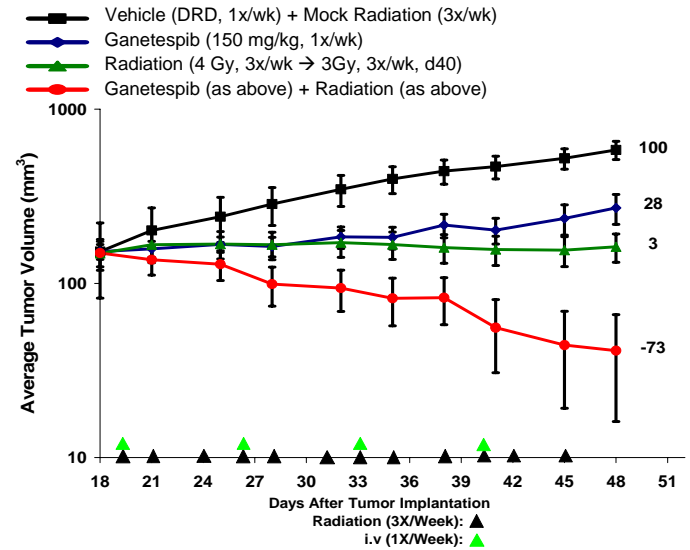
INHIBITION OF RESISTANCE MECHANISMS

Ganetespiib + Paclitaxel

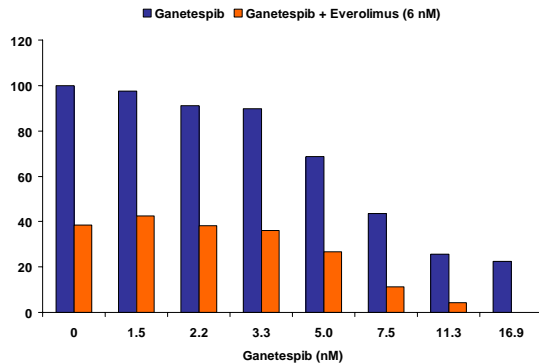
Normalized Isobologram



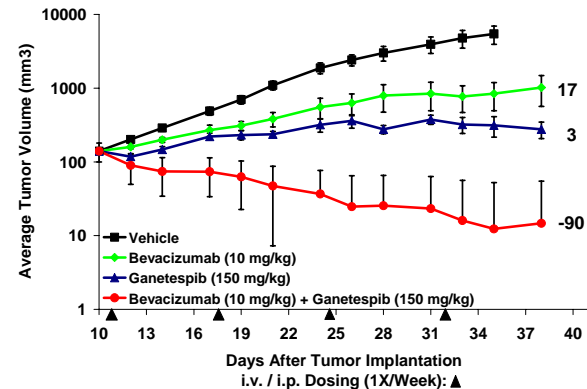
Ganetespiib + Radiotherapy



Ganetespiib + mTOR inhibitor



Ganetespiib + Avastin



Opportunity

Approach	# Patients (US)	Examples
Single-agent biomarker-defined subpopulation	~5,000	<ul style="list-style-type: none">• Crizotinib (Pfizer ALK inhibitor)• PLX4032 (Roche-Plexxikon BRAF inhibitor)
Combination broader population	~500,000	Taxanes, platinum

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