Charting Our Own Course:
The First Annual Exelixis R&D Day

EXELIXIS™

December 6, 2005
Four Seasons Hotel, New York, NY

Forward-Looking Statement

Please note that the following presentation and discussion contains certain statements that are forward-looking, including our estimated future revenues and expenses as well as our estimated future balances of cash, cash equivalents, short-term investments, investments held by Symphony Evolution and restricted cash. These statements are only predictions and involve risks and uncertainties. Our actual results and the timing of events could differ materially from those anticipated in our forward-looking statements as a result of these risks and uncertainties, which include the potential failure of our product candidates to demonstrate safety and efficacy in clinical testing; our ability to complete Phase 1 and initiate Phase 2 at the referenced times; our ability to conduct the Phase I clinical trials of XL999, XL784, XL647, XL880, XL820, XL844 and XL184 sufficient to achieve positive completion; and the therapeutic and commercial value of our compounds. These and other risk factors are discussed under "Risk Factors" in our current Quarterly Report and other SEC reports. We disclaim any obligation to release publicly any updates or revisions to any forward-looking statements.

Charting Our Own Course

1:00	Uncommon Approach, Extraordinary Results	George Scangos, President & CEO
1:15	Moving Fast, Thinking Large – XL999,XL647,XL880, XL784	Michael Morrissey, SVP Jeff Latts, SVP Ian Malcolm, VP
3:00	Break	
3:15	New Targets, New Opportunities – XL820, XL844, XL184, XL281, XL418, XL228, LXR/FXR/MR	Michael Morrissey, SVP Jeff Latts, SVP
4:45	Growing from a Solid Financial Foundation	Frank Karbe, SVP & CFO
4:55	Charting Our Own Course	George Scangos, President & CEO
5:00	Management Panel Q & A	All
5:30	Close & Reception	

Uncommon Approaches, Extraordinary Results

Extraordinary productivity - 13 compounds in development since 2003

- Internally generated
- Renewable
- High-quality

Rapid progress

- 1 compound in phase III
- 4 compounds soon to be in phase II
- 3 compounds in phase I
- 5 compounds in preclinical development

Solid business performance

- Year end 2004 cash $170 million
- Year end 2005 cash >$200 million

Many upcoming key events

Exelixis as a Major Cancer Company

Generate and renew pipeline of high-quality compounds

- 3 INDs per year

Take forward some compounds independently

- 9 out of 12 compounds from GSK collaboration
- Non-GSK compounds

Partner opportunistically

- Balance near term cash and long-term upside
- Cancer and metabolism
- Partner to balance cash needs
- Increase equity ownership in compounds over time

Bring better therapies to cancer patients

Charting Our Own Course

High-quality pipeline

- Best in class
- First in class

High-quality team

- Discovery
- Development
- Finance
- Marketing

Critical mass

Execution

- Move pipeline forward aggressively
- Renew pipeline
- Keep company adequately financed

Continual questioning of accepted dogma

Rapid entry into marketplace

Exelixis 2005 Business Accomplishments

Amended GSK Agreement	**January**
Completed Integration of X-Ceptor	**February**
Amended GenOptera Agreement	**April**
$35 Million GSK Milestone	**May**
Genentech Notch Collaboration	**June**
Symphony Transaction	**June**
Helsinn Partnership for XL119	**June**
$50 Million Equity Offering	**August**
BMS LXR Collaboration	**December**

Increased Cash Position

Exelixis 2005 R&D Accomplishments

New Development Compounds

- XL228, XL418, XL281, XL335, XL550

Phase I Initiation

- XL880, XL820, XL184, XL844

Phase I Objectives Achieved

- XL999, XL647, XL784

Phase II Initiation

- XL999

Phase III Multinational Trial

- XL119

New Exelixis BMS Collaboration on LXR

Discover, develop and commercialize novel therapies targeted against the Liver X Receptor (LXR)

- NHR with significant potential as a new class of medicines in cardiovascular and metabolic disorders
- Exelixis discovered multiple proprietary LXR agonist drug candidates that are highly potent, selective and efficacious in animal models of atherosclerosis

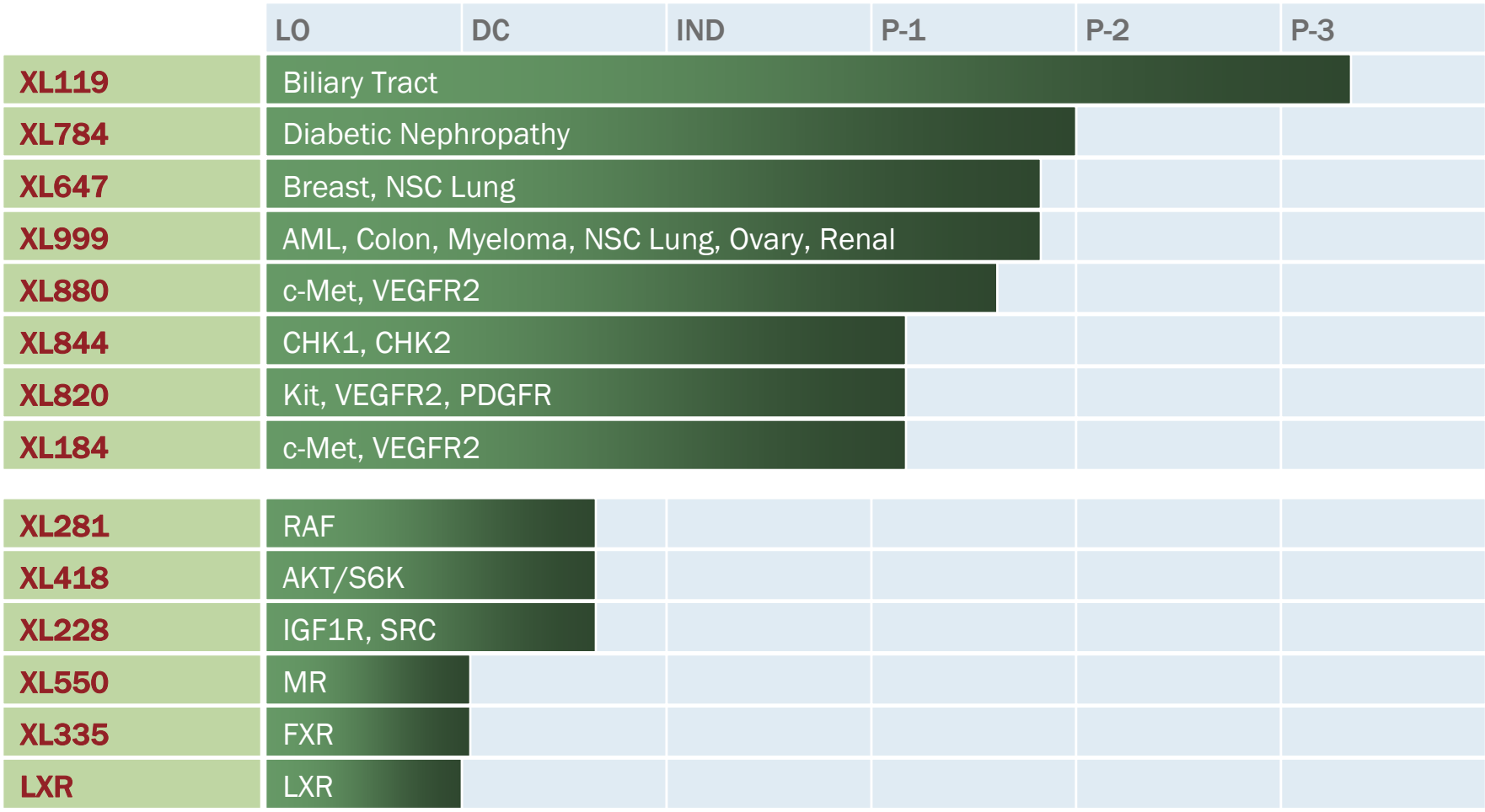
Combines Exelixis discovery and early biology expertise with BMS development and commercialization capabilities

- Jointly identify candidates for IND enabling studies
- BMS to undertake further development and commercialization

Significant financial terms

- Upfront payment: $17.5 million
- R&D funding: $10 million per year (initial term 2 years)
- Development & regulatory milestones of approximately $140 (for each of up to 2 products)
- Sales milestones & royalties

Exelixis Pipeline



Moving Fast, Thinking Large:
XL999, XL647, XL880 and XL784

Exelixis: R&D Strategy

Build Leading Oncology Product Portfolio

Pipeline of "first-in-class" & "best-in-class" compounds

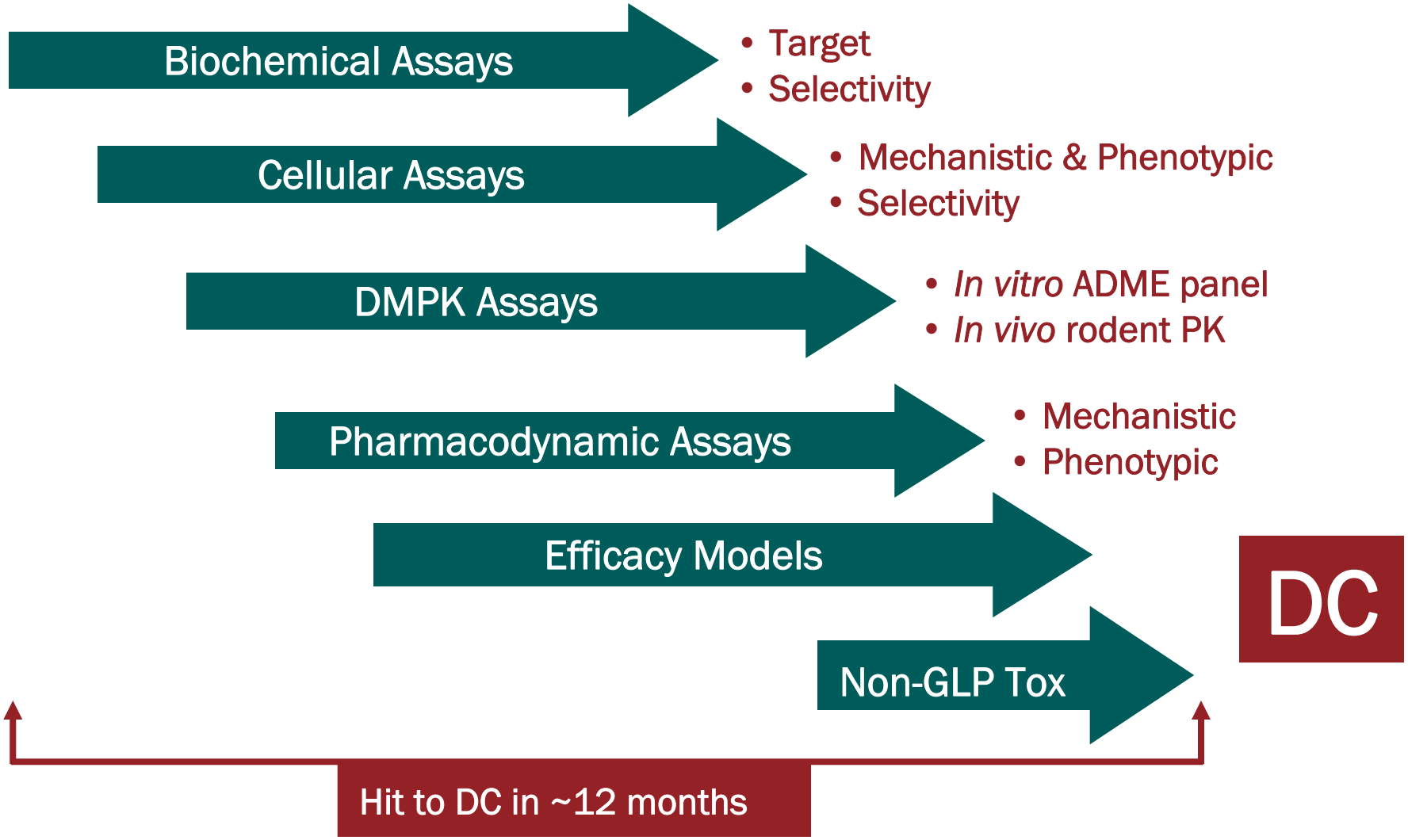
- Industrialized drug discovery
- HTS lead to IND in 2 years
- Broad Phase II programs to maximize success in Phase III

HTS Lead to DC in <12 months

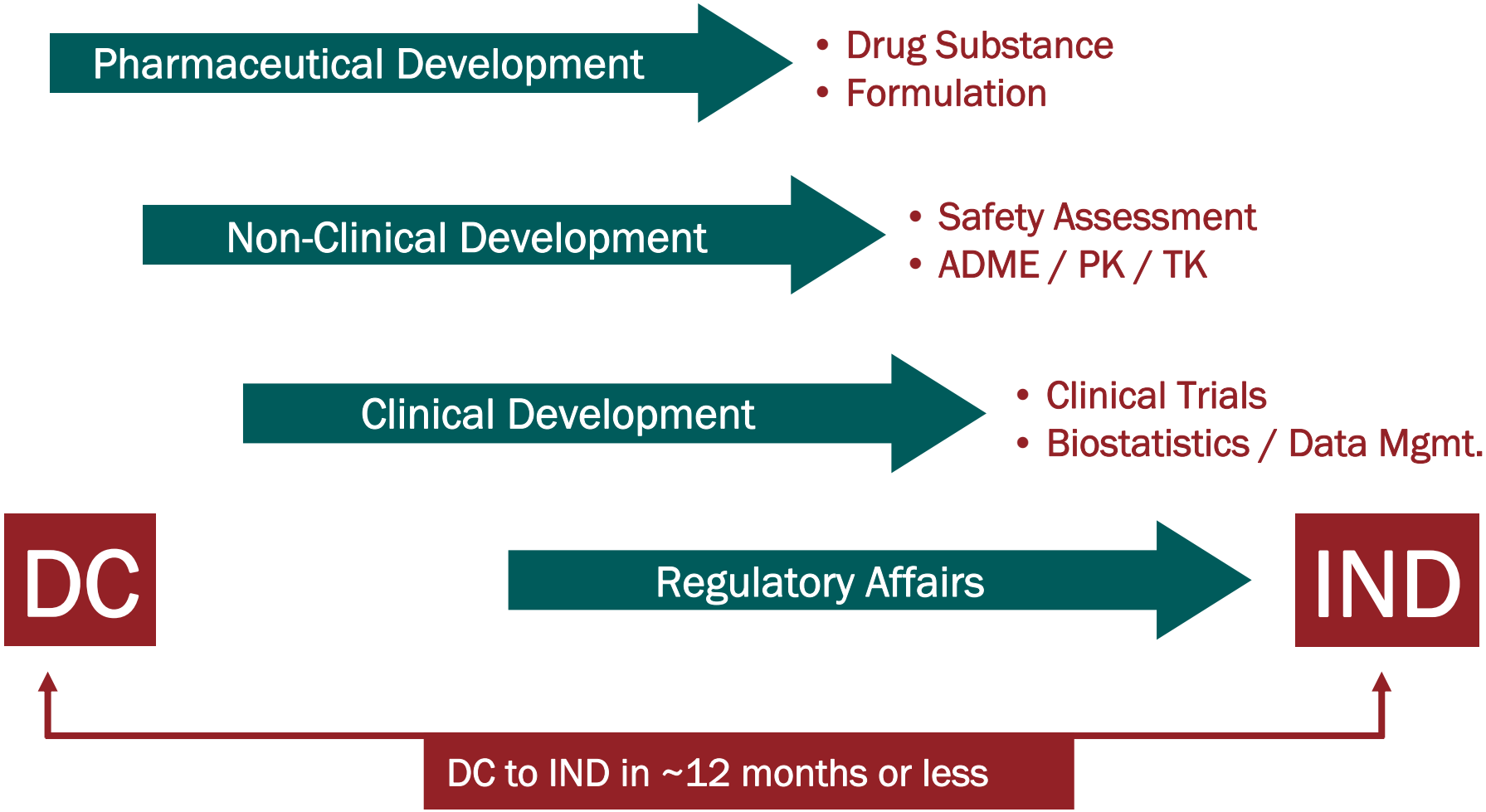
- Lead discovery = multiple novel chemotypes with low nM potency, selectivity and good initial DMPK properties
- Early in vivo characterization (PK, PD & efficacy)
- Rapid optimization of key liabilities assisted by structural biology

Unwavering focus on execution: speed & quality

Parallel Lead Optimization



Development at Exelixis



Dosing Regimens in Oncology

INTERMITTENT

May permit more intensive dosing

- Particularly for drugs expected to show tumor regression

Generally faster route to IND and demonstration of efficacy

- Permits more rapid dose escalation

Classically used for drugs with narrow therapeutic window

- Typically dosed at MTD
- Allows for recovery of normal tissues between cycles

CONTINUOUS

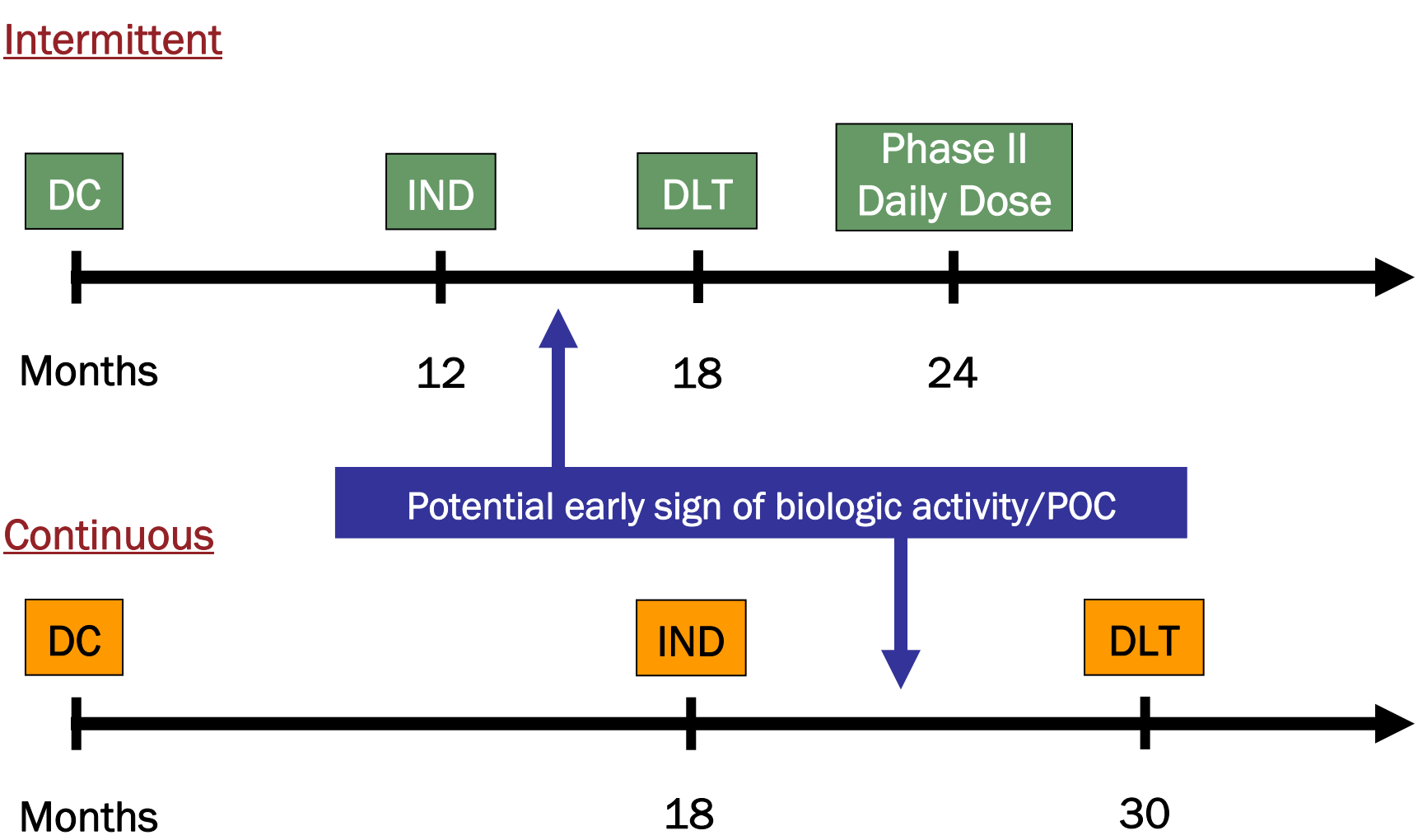
Most commonly associated with drugs that are expected to show tumor growth inhibition

Slower initial development may be offset by smoother transition to registration trials

May elicit different side effect profile with continuous exposure

- Dose may be selected based on indicators of biological activity

Rationale for Selection of Intermittent Dosing Regimen in Early Development



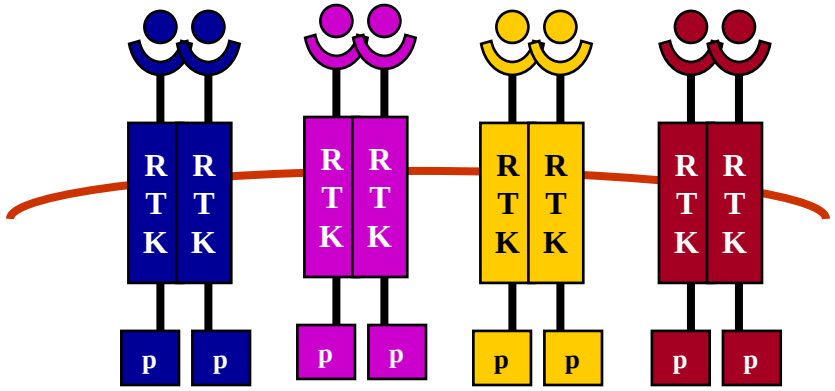
Exelixis Kinase Inhibitors for Oncology

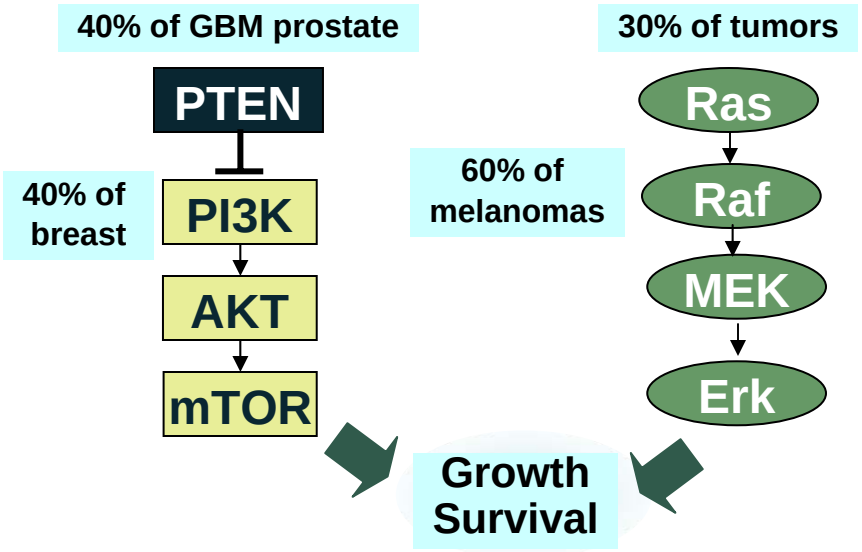
EXEL 1st Generation Inhibitors

- SS-RTK Inhibitors that target multiple RTKs
- Expedite clinical POC by targeting RTK activating mutations

EXEL 2nd Generation Inhibitors

- RTK signaling pathway inhibitors
- Target mutationally-activated pathways downstream of RTKs





Spectrum Selective Kinase Inhibitors™

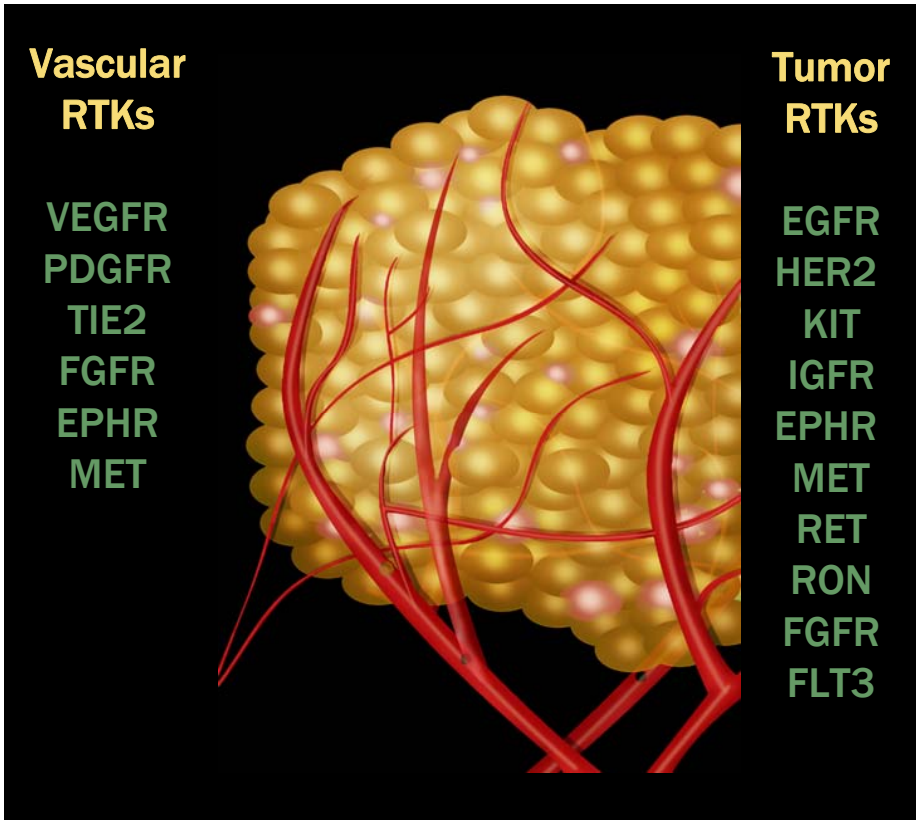
Maximize efficacy by simultaneous inhibition of multiple RTKs

- Biological impact on tumor & vasculature

Unique RTK inhibition profiles for different tumor types

- Polygenic disease – many solutions required

Address different tumor types based on known molecular alterations (e.g. RTK mutations)



XL999 Summary

Low nM potency vs VEGFRs, PDGFRs & FGFRs

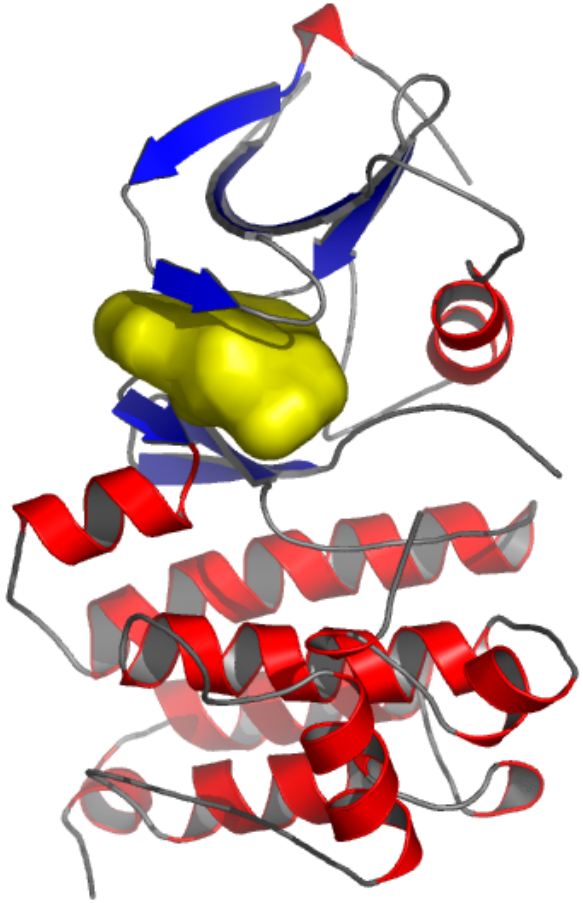
Rapid and selective destruction of tumor vasculature

Potent anti-tumor activity

- Solid tumors
- FLT3-driven leukemia

Optimized for pharmaceutical properties

- Low CYP450 inhibition and high aqueous solubility
- Excellent PK/PD properties



XL999 Rationale

Simultaneous inhibition of 3 key mediators of tumor vessel development and survival

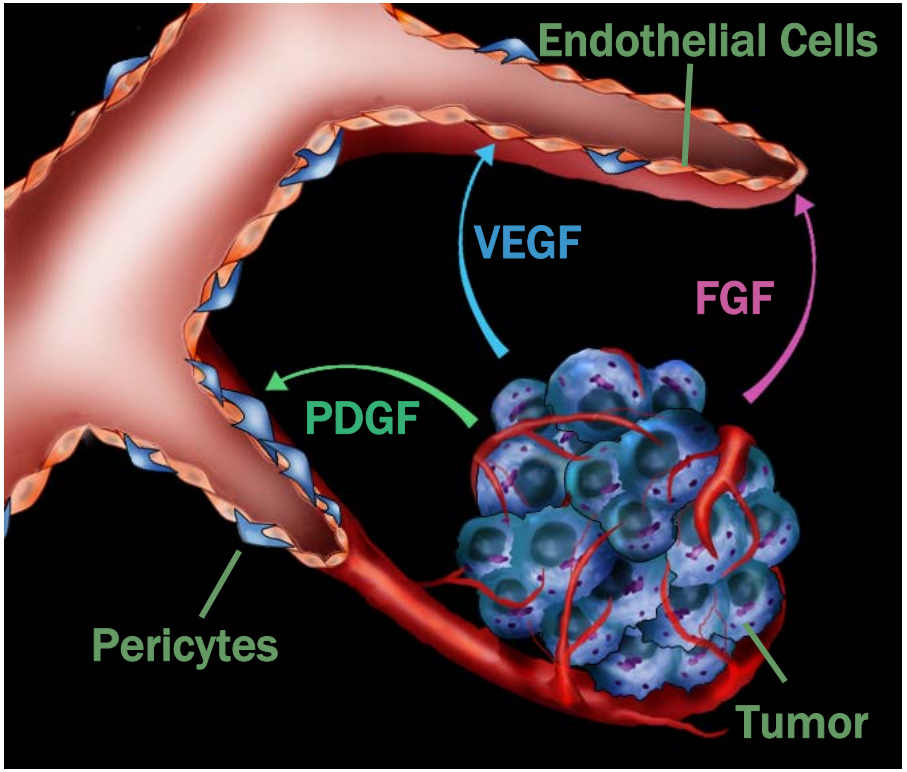
- VEGFR, FGFR and PDGFR

Dual inhibition of VEGFR and PDGFR more effective in preclinical model

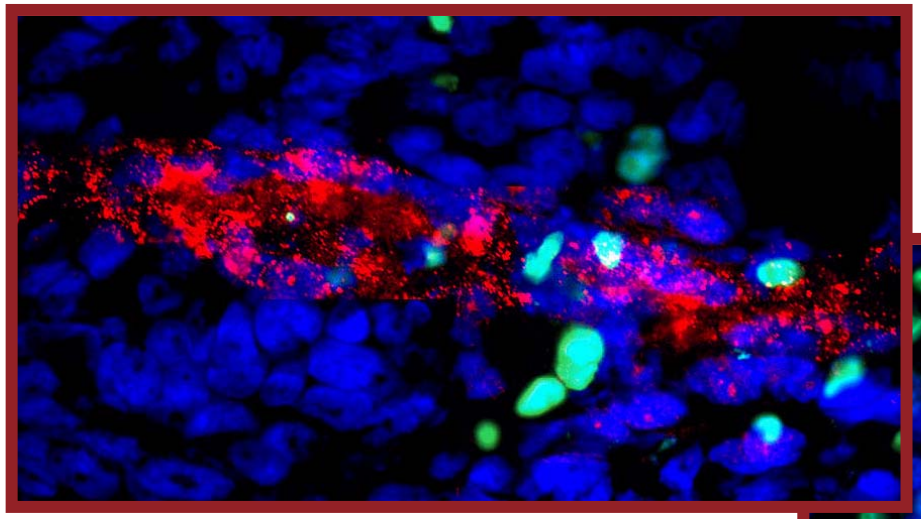
- Bergers et al 2003

Tumors can escape VEGF blockade by activating FGF production

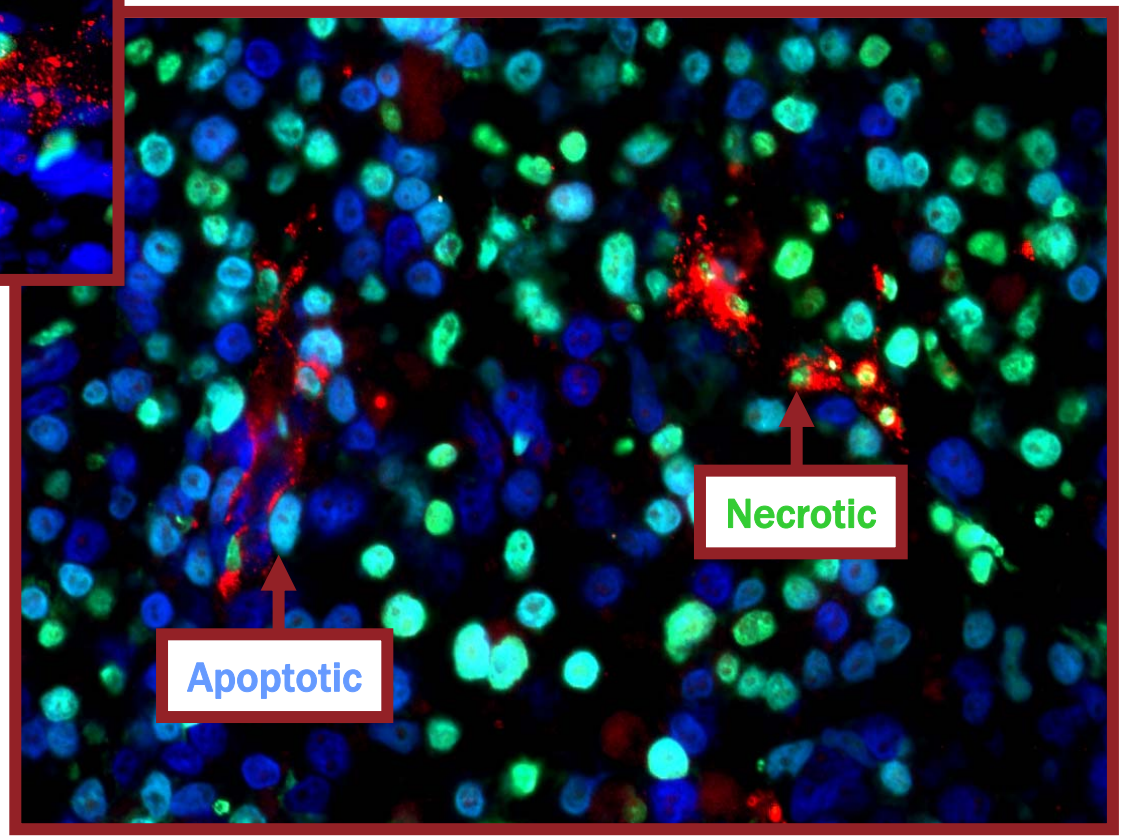
- Casanovas et al 2005



Rapid Induction of Cell Death by XL999



DAPI
MECA-32
TUNEL



Very rapid onset (~4 hr) of tumor and endothelial cell apoptosis

XL999 is a Potent Inhibitor of Mutationally-Activated Kinases

FGFR3 is overexpressed in 15% of multiple myeloma patients

- patients have a poor prognosis

FLT3 is activated by mutation in 30% of AML patients

- FLT3/ITD mutations occurs in 25% of patients

RET is activated by point mutation in familial multiple endocrine neoplasia type 2 (MEN) and medullary thyroid carcinoma

- activating rearrangements occur in sporadic papillary thyroid carcinoma

XL999 is a low nM inhibitor of FGFR3, FLT3 & RET kinases

XL999-001 – Phase I Study Design and Subjects

Phase I, nonrandomized, open-label, dose-finding study

Adults (aged ≥18 years) with:

- Histologically confirmed metastatic or unresectable solid tumors
- ECOG performance status ≤2
- Life expectancy >3 months
- Adequate hematologic, renal, and hepatic function

Treatment

- Single 4-hour IV infusion of XL999 on Day 1
- 14 day treatment cycles
- Dose escalation allowed only in the absence of any drug-related adverse events Grade 2 or higher at the previous dose

XL999-001 – Safety Results

Data as of June 3, 2005

ADVERSE EVENT	% OF PATIENTS	
	GRADE 1 OR 2	GRADE 3 OR 4
Hypertension	35	
Increased LFTs	17	13
Neuropathy	17	
Fatigue	17	
Dizziness	13	
Nausea	13	
Vomiting	9	
Myalgia	9	
Arthralgia	9	
Perioral dyesthesias	9	

Data Presented at EORTC-AACR-NCI Meeting, November 2005

XL999-001 – Safety Results

All toxicities (except transaminase changes) resolved within 24 hours

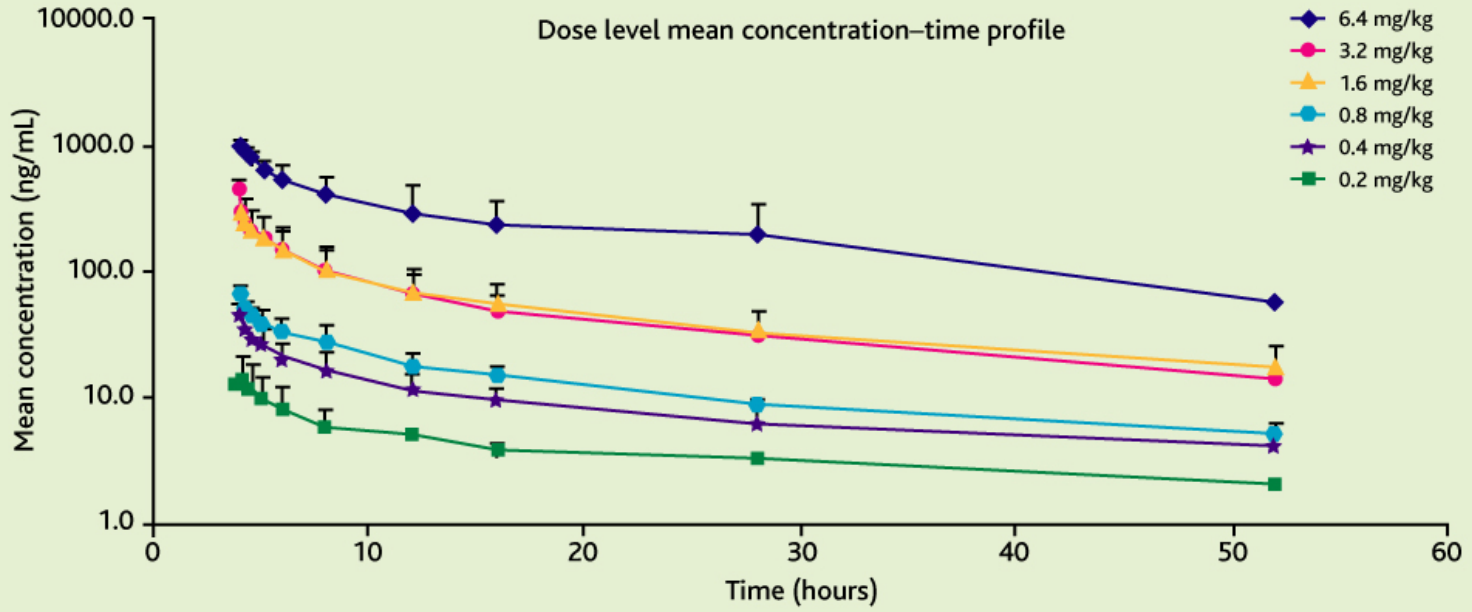
2 patients received 6.4 mg/kg dose and experienced hypertension and grade 3/4 elevations in hepatic transaminases; 1 of the 2 patients experienced heart failure

MTD is 3.2 mg/kg

Data Presented at EORTC-AACR-NCI Meeting, November 2005

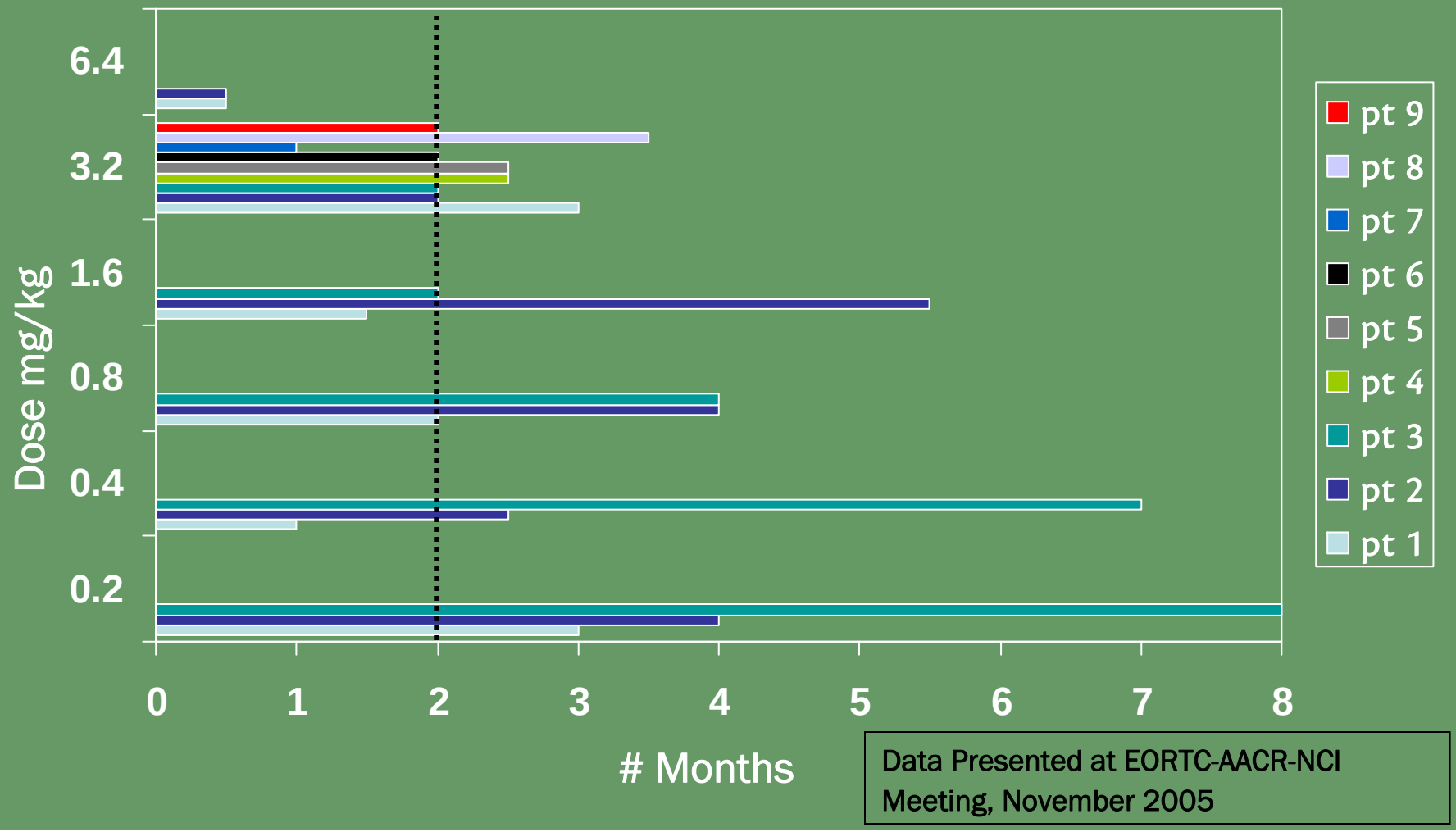
XL999-001 – Pharmacokinetics

Elimination was linear, with an elimination half-life for all dose levels of ~24 hours (range 12–42 hours)



Data Presented at EORTC-AACR-NCI Meeting, November 2005

Study XL999-001 – Duration of Therapy
As of June 30, 2005



Data Presented at EORTC-AACR-NCI Meeting, November 2005

XL999-001 – Tumor Response

Of the 22 evaluable patients followed for ≥8 weeks:

- 2 partial responses (1 confirmed)
- 1 minor response (28% reduction)
- 4 patients with stable disease for 3–7 months

RESPONSE	NUMBER OF PATIENTS	PRIMARY DIAGNOSIS
Complete response	0	
Partial response (confirmed)	1	Squamous cell cancer of the liver
Partial response (unconfirmed)	1	Thyroid carcinoma
Minor response	1	Renal cell carcinoma
Stable disease	4	Thyroid carcinoma (N=2)
		Renal cell carcinoma (N=2)
Progressive disease	15	Various

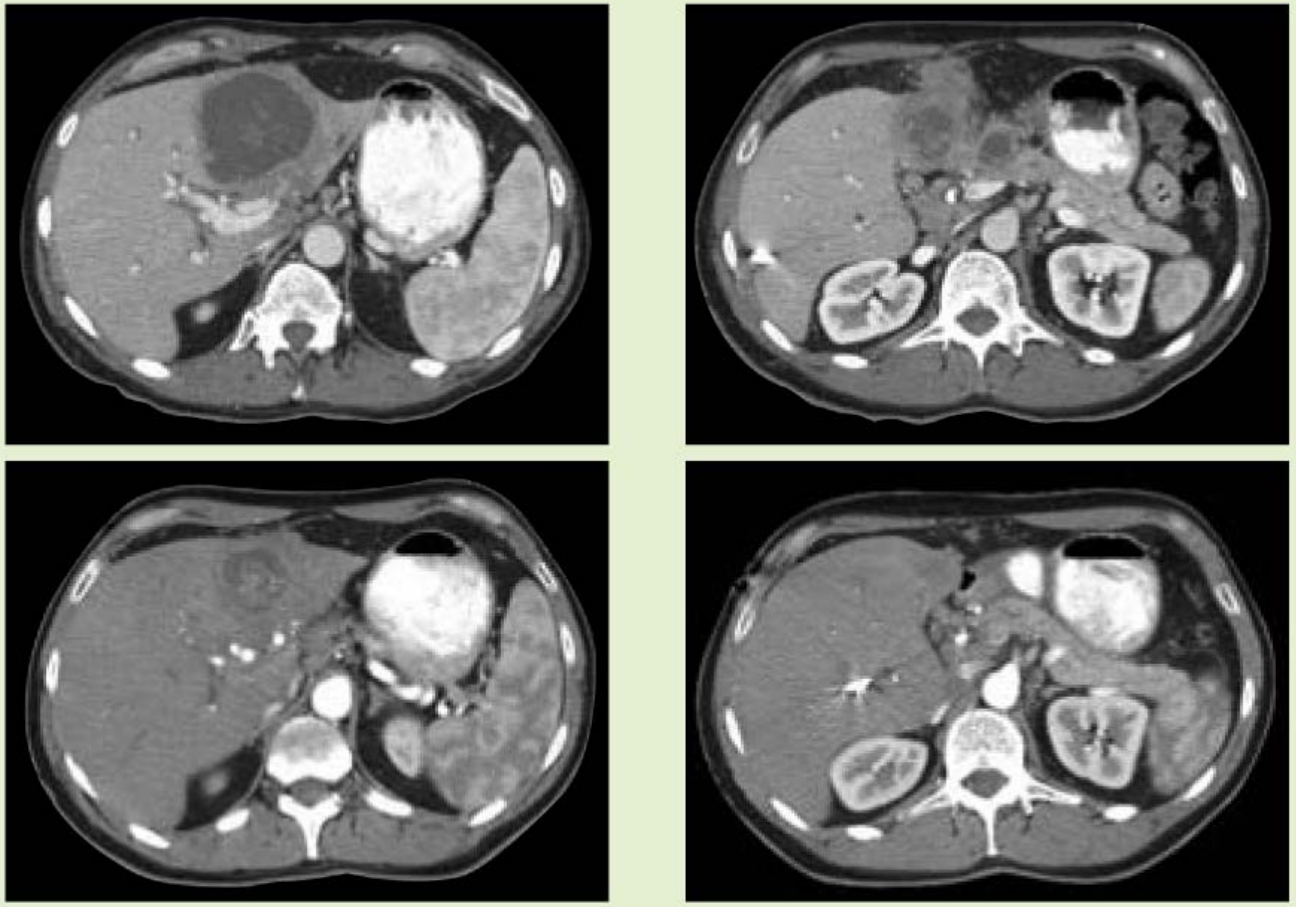
Data Presented at EORTC-AACR-NCI Meeting, November 2005

XL999-001 – Tumor Response

Partial response in a patient with squamous cell liver cancer

Pre-treatment

Post-treatment
(3 months)



Data Presented at EORTC-AACR-NCI Meeting, November 2005

XL999-001 – Conclusions

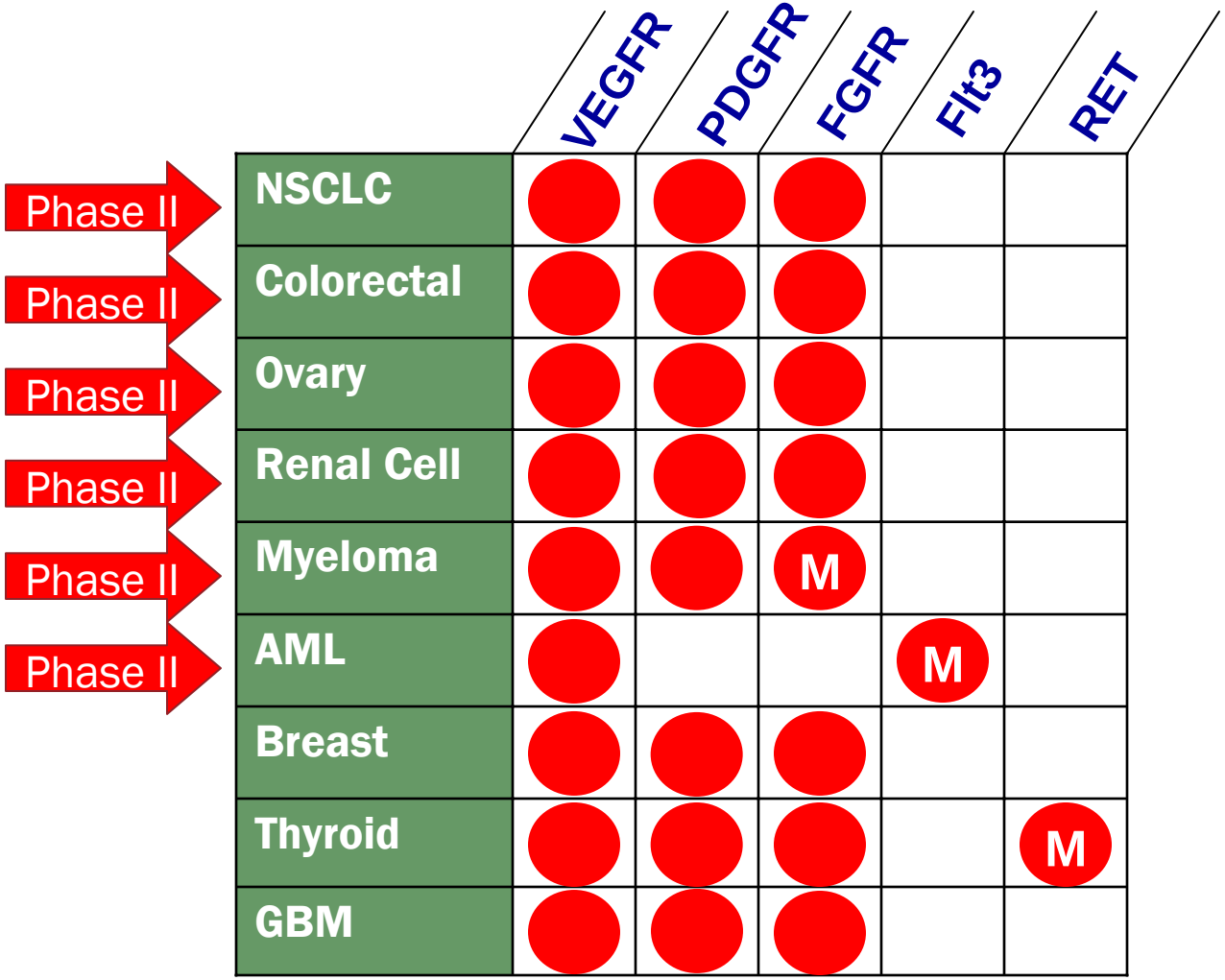
A single dose of XL999 at 3.2 mg/kg was generally well tolerated

XL999 administered at 2-weekly intervals showed preliminary evidence of clinical activity with no cumulative toxicity

Based on safety and pharmacokinetic data, a weekly dosing schedule is now being evaluated

Data Presented at EORTC-AACR-NCI Meeting, November 2005

XL999 – Potential Development Profile



A Phase II Study of XL999 in Subjects with Metastatic Non-small Cell Lung Cancer

Target Population	Patients with metastatic non-small cell lung cancer who have received prior platinum or taxane therapy
Study Design	Phase II non-randomized, open label
Objectives	Primary: determine confirmed response rate; evaluate safety and tolerability Secondary: determine PFS, OS, Duration of Response; further characterize PK and PD
Dose/route/regimen	2.4 mg/kg as a 4 hour IV infusion weekly
Number of Subjects	Two-stage design; 17 patients initially enrolled, if ≥1 response, enroll total of 40 patients
Study Length	15 months for patient accrual and treatment
Assessments	Efficacy: at baseline and every 8 weeks; responses confirmed at approximately 30 days

Phase II Studies for XL999

Tumor Type	Target Population
Non Small Cell Lung Cancer	Patients with metastatic NSCLC who have received prior platinum or taxane therapy
Metastatic Colorectal Carcinoma	Patients with MCC who have received at least one prior therapy regimen
Recurrent Ovarian Carcinoma	Patients with recurrent ovarian cancer who have or have not previously received a platinum based regimen
Metastatic RCC	Patients with or without prior therapy
Relapsed/Refractory Multiple Myeloma	Patients with MM refractory to or relapsed after two prior chemotherapeutic or biologic therapies
Acute Myeloid Leukemia	Patients with AML who have not received prior therapy or have received at least two chemotherapy regimens

Exelixis Discovery and Development Provide Solid Framework for Commercial Success

Early Market Entry

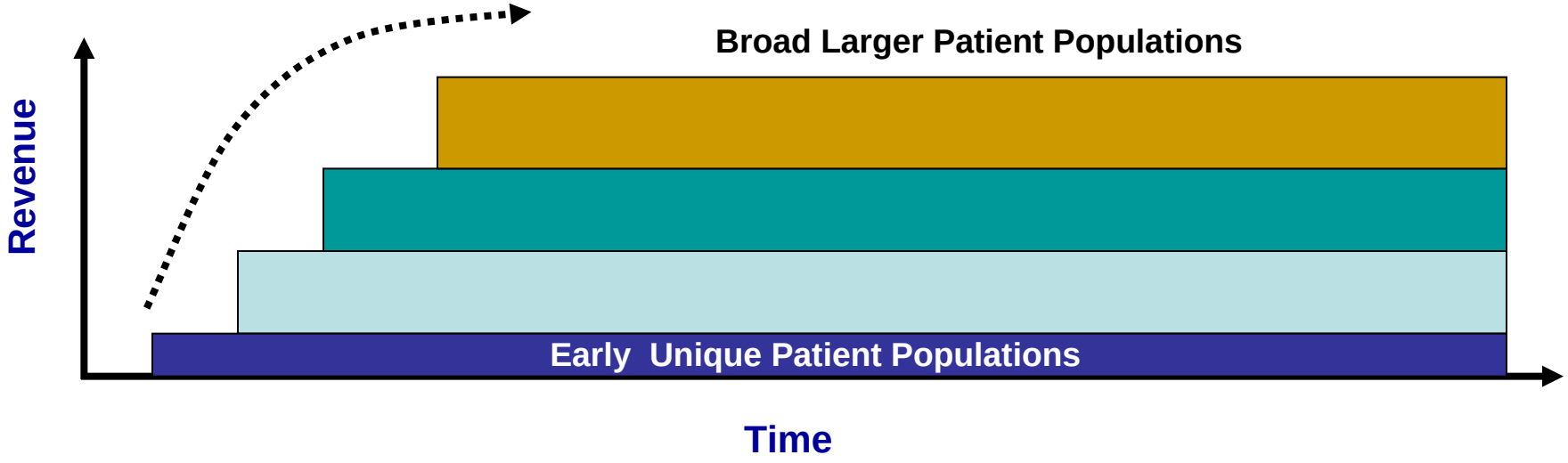
Targeted Development in Unique Patients

- In diseases driven by specific target or where current therapies are rendered ineffective due to target modification

Access Significant Patient Populations

Broad Development in Major Tumors

- In indications where targets are validated in prevalent tumor types



First-in-class or best-in-class profiles drive market success

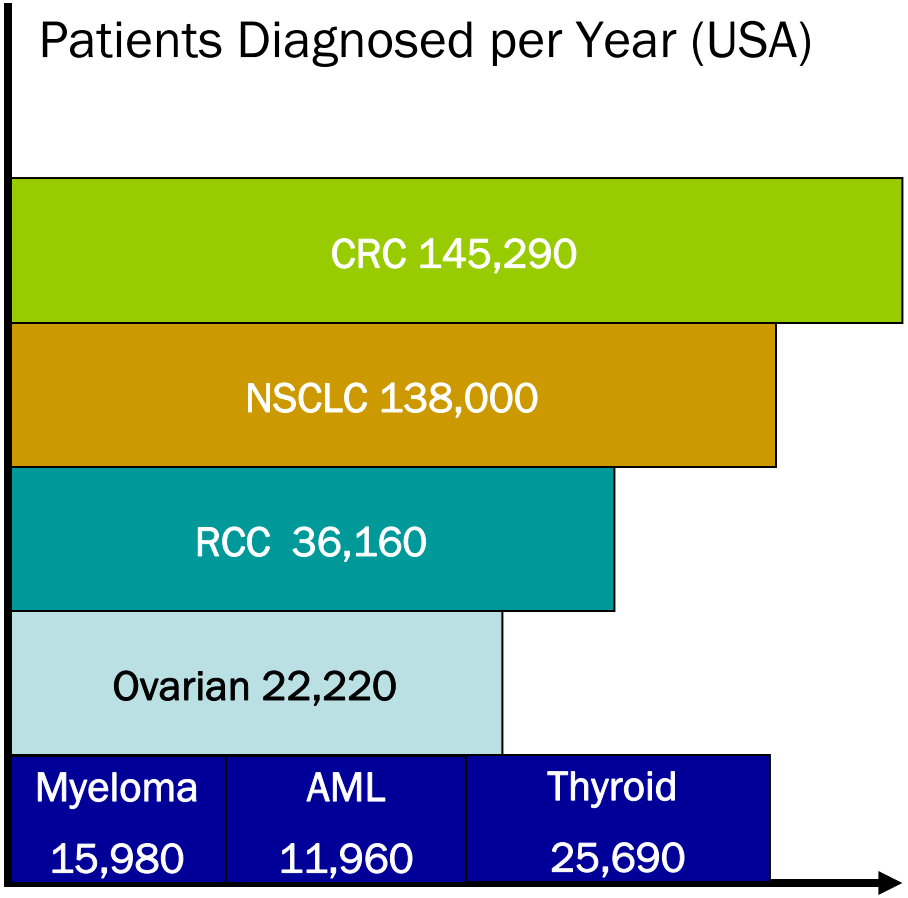
XL999 – Market Entry and Expansion

1. Early Market Entry Points

- Multiple Myeloma: FGF targeting
- AML: FLT3 targeting
- Thyroid: RET targeting

2. Market Expansion

- VEGFR, PDGFR, FGFR
- Prevalent tumor types:
  - NSCLC, CRC, Ovarian



Incidence based on ACS Facts & Figures 2005

XL647 Summary

Low nM inhibition of kinase spectrum

- VEGFR2, EGFR, HER2
- Activity against activating EGFR mutations and Tarceva resistant EGFR mutant

Exceptional pharmaceutical properties

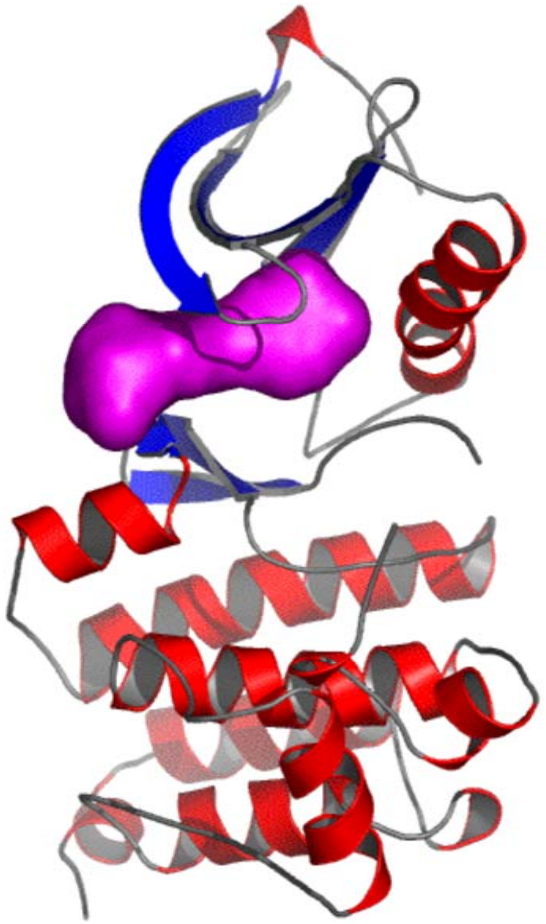
- High solubility & metabolic stability

Excellent drug metabolism & pharmacokinetics properties

- High oral bioavailability, long $T_{1/2}$

Potent activity in multiple xenograft models

- Long duration of action after single oral dose
- Effects on tumor and tumor vasculature



XL647 - Rationale

Potent inhibition of kinase spectrum:

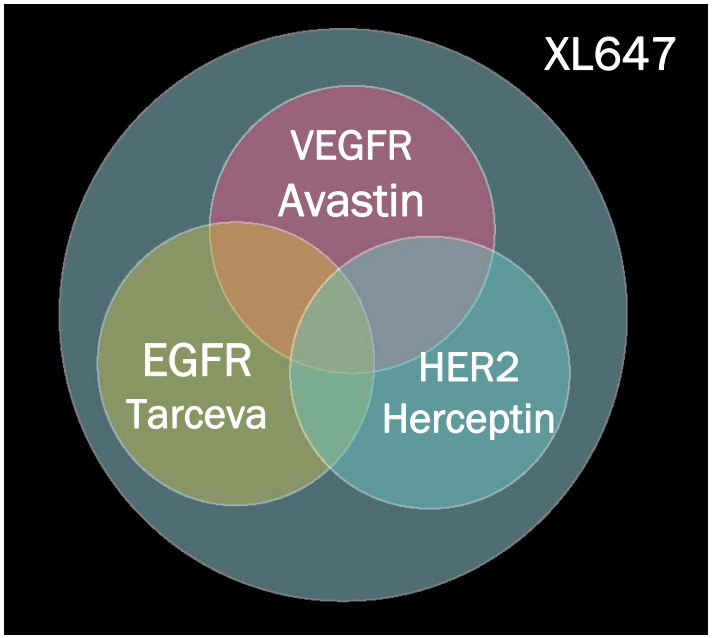
- VEGFR2, EGFR and HER2

Inhibition of multiple EGFR family members

- Co-expression of family members occurs in tumors
- May circumvent acquisition of resistance through upregulation of alternate family members

Simultaneous inhibition of 3 clinically validated kinases

- Early clinical data with combinations of VEGFR and EGFR inhibitors promising



XL647-001 – Study Design and Subjects

Phase I, nonrandomized, open-label, dose-finding study

Adults (aged ≥18 years) with:

- histologically confirmed metastatic or unresectable solid tumors
- ECOG performance status ≤2
- life expectancy >3 months
- adequate hematologic, renal, and hepatic function

Oral dosing of XL647 on Day 1 followed 72 hours later (Day 4) by 5 consecutive daily oral doses

XL647-001 – Study Population Baseline Characteristics

To date, 31 patients have been enrolled and are evaluable for safety analysis

CHARACTERISTIC	NUMBER OF PATIENTS
Median age, years (range)	56 (33–75)
Gender (male/female)	18/13
Race	
Caucasian	26
Black	1
Asian	3
Pacific Islander	1
Diagnosis	
Lung	10
Colon/rectum	4
Renal cell carcinoma	3
Other	14
Secondary lesions	
Bone	10
Liver	11
Lung	23
Lymph nodes	11
Skin	1
Other	13
Measurable disease	26
Prior chemotherapy	
Median number of regimens (range)	2 (0–8)

Data Presented at EORTC-AACR-NCI Meeting, November 2005

XL647-001 – Summary Of Treatment Status At Cut-off

Data as of October 12, 2005

STATUS		NUMBER OF PATIENTS
On-treatment		7
Off-treatment		24
Reason for withdrawal		
Progressive disease		22
SAE (unrelated)		2
DOSE LEVEL ACHIEVED (mg/kg)	**N**	**NUMBER OF CYCLES**
0.06	3	3–19
0.12	3	3–7
0.19	3	2–3
0.28	3	5–21 (ongoing)
0.39	3	4–9
0.78	3	2–15 (ongoing)
1.56	3	4–11
3.12	7	1–4
4.68	3	Ongoing

SAE — serious adverse event.

Data Presented at EORTC-AACR-NCI Meeting, November 2005

XL647-001 – Adverse Events

ADVERSE EVENT	PERCENT OF PATIENTS	
	GRADE 1 OR 2	GRADE 3 OR 4
Fatigue	32	
Nausea	26	
Diarrhea	26	
Rash	19	
Vomiting	10	
Paresthesias	6	
Anemia		6

Data Presented at EORTC-AACR-NCI Meeting, November 2005

XL647-001 – Safety Results

1 serious adverse event "possibly related"

- 1 case of Grade 4 pulmonary embolism at the 3.12 mg/kg dose, considered 'possibly related to study treatment'

2 dose-limiting toxicities:

- 1 episode of QTc prolongation at 3.12 mg/kg
- Grade 3 diarrhea at 7.0 mg/kg

Data Presented at EORTC-AACR-NCI Meeting, November 2005

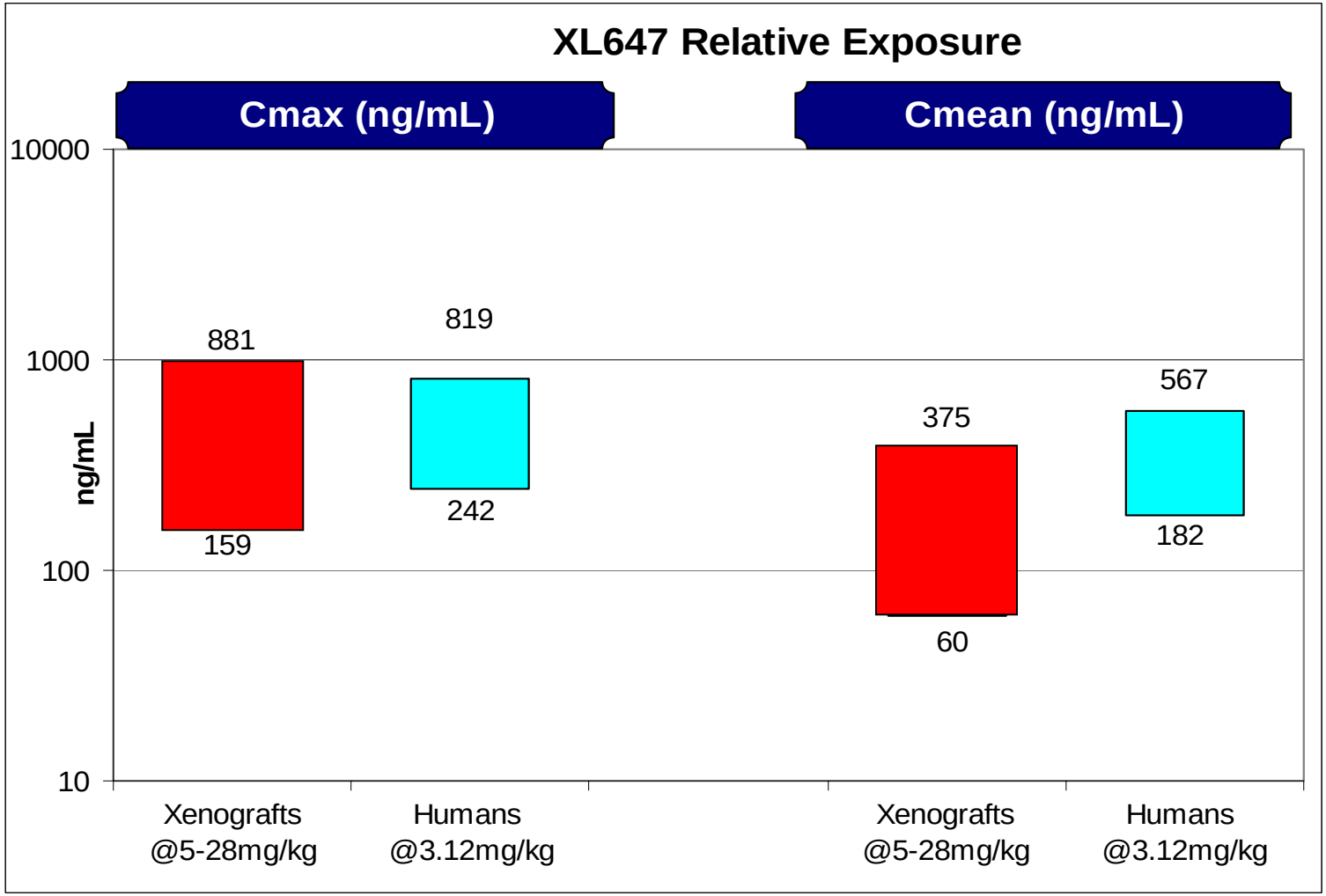
XL647-001 – Pharmacokinetics

Plasma XL647 concentrations increased with dose (range: 0.06–3.12 mg/kg) and with duration of dosing

Terminal half-life values were approximately 70 hours following consecutive dosing days, and did not appear to change with dose level

Data Presented at EORTC-AACR-NCI Meeting, November 2005

XL647 Relative Exposure



XL647-001 – Clinical Efficacy

1 patient with a primary diagnosis of non-small cell lung cancer (NSCLC) has achieved a partial response

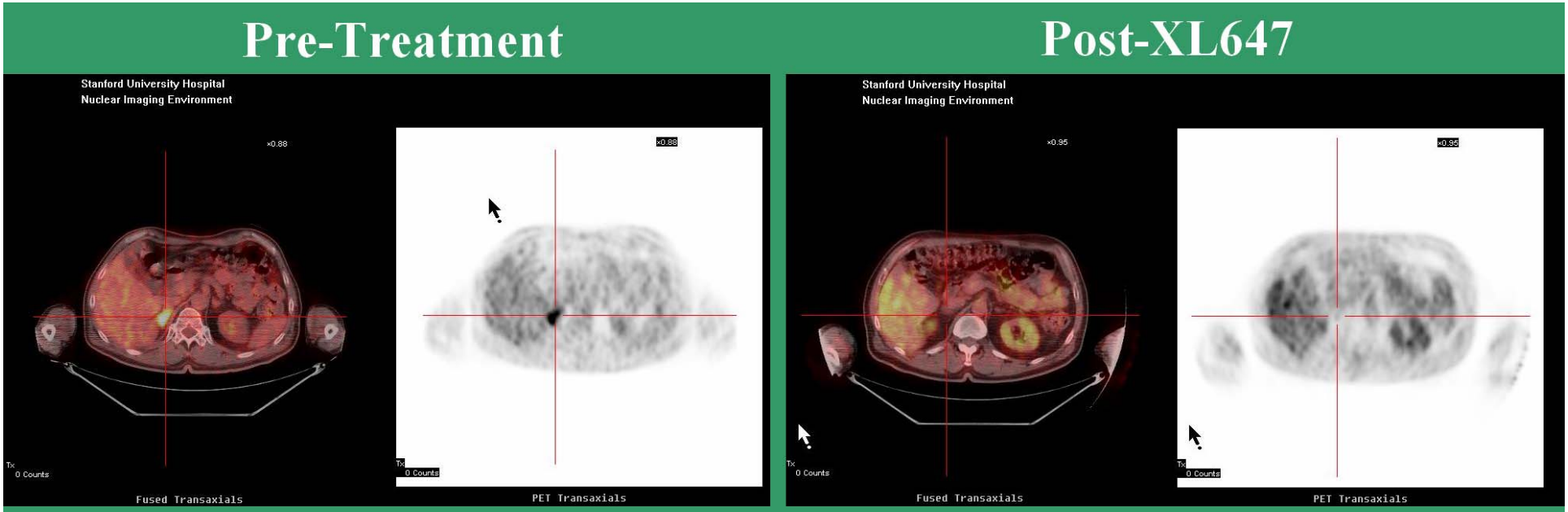
7 patients (primary diagnoses: NSCLC [n=2], chordoma [n=2], adenoid cystic carcinoma, adrenalcortical carcinoma, colorectal) have achieved prolonged stable disease (>3 months)

RESPONSE	NUMBER OF PATIENTS	PRIMARY DIAGNOSIS	DURATION OF STABLE DISEASE (MONTHS)
Complete response	0		
Partial response[a]	1	NSCLC	
Stable disease	7	NSCLC (2) Cordoma (2) Adrenalcortical carcinoma (1) Adenoid cystic carcinoma (1) Colorectal (1)	5+ and 10+ 7+ and 8 4.5 7+ 3.5
Progressive disease	16	Various	
Unevaluable or too early	7	Various	

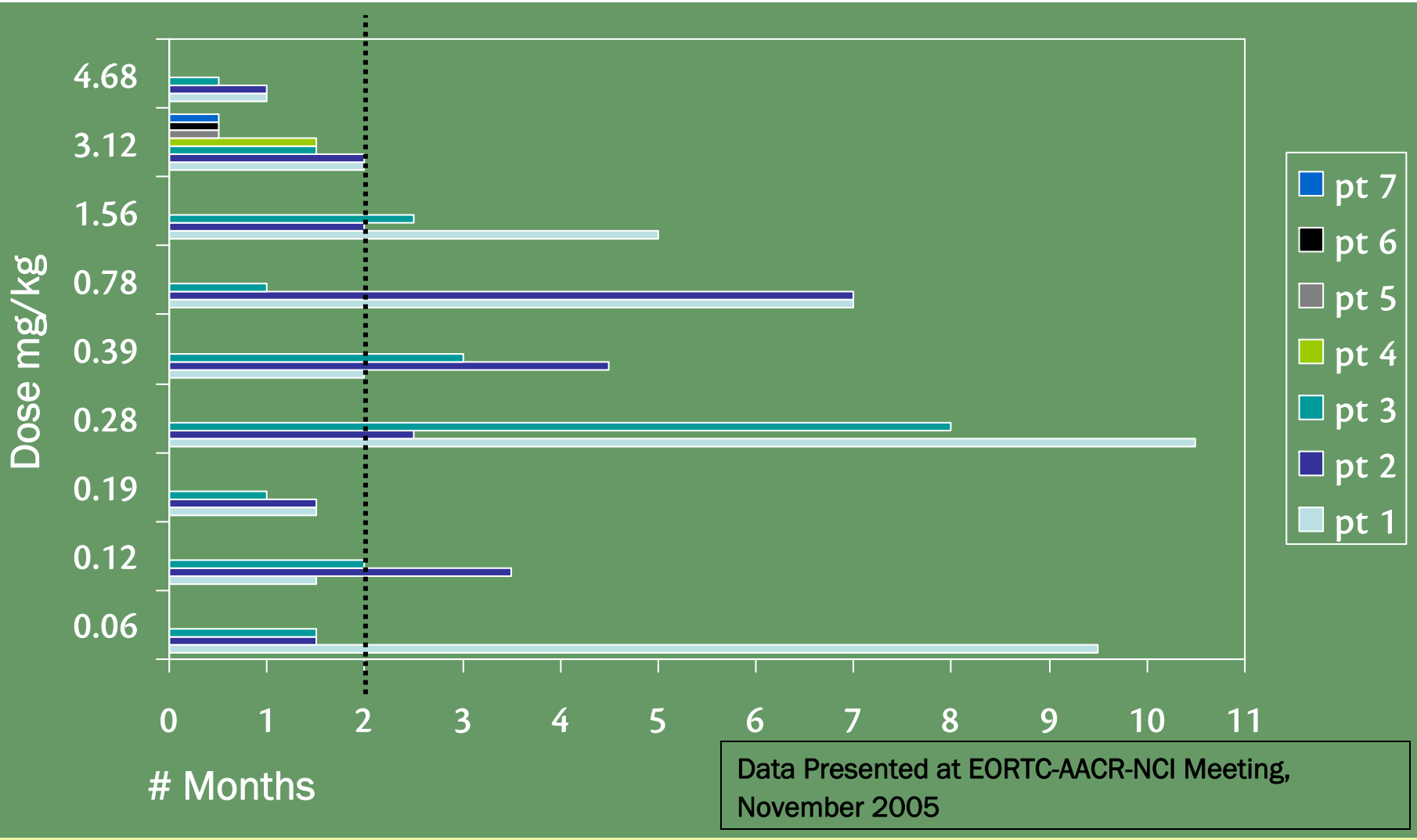
NSCLC — non-small cell lung cancer.
[a]Patient on study for 9 months and achieved a partial response prior to eventual progression.

Data Presented at EORTC-AACR-NCI Meeting, November 2005

XL647-001 – Tumor Response



Study XL647-001 – Duration of Therapy
As of October 12, 2005



XL647-001 – Summary

Oral SSKI targeting clinically validated kinase receptors – VEGFR2, HER2, EGFR

Clinical signals of activity in phase I – 1PR, 7 SD (> 3months)

DLT of Gr. 3 diarrhea reported at 7.0 mg/kg dose

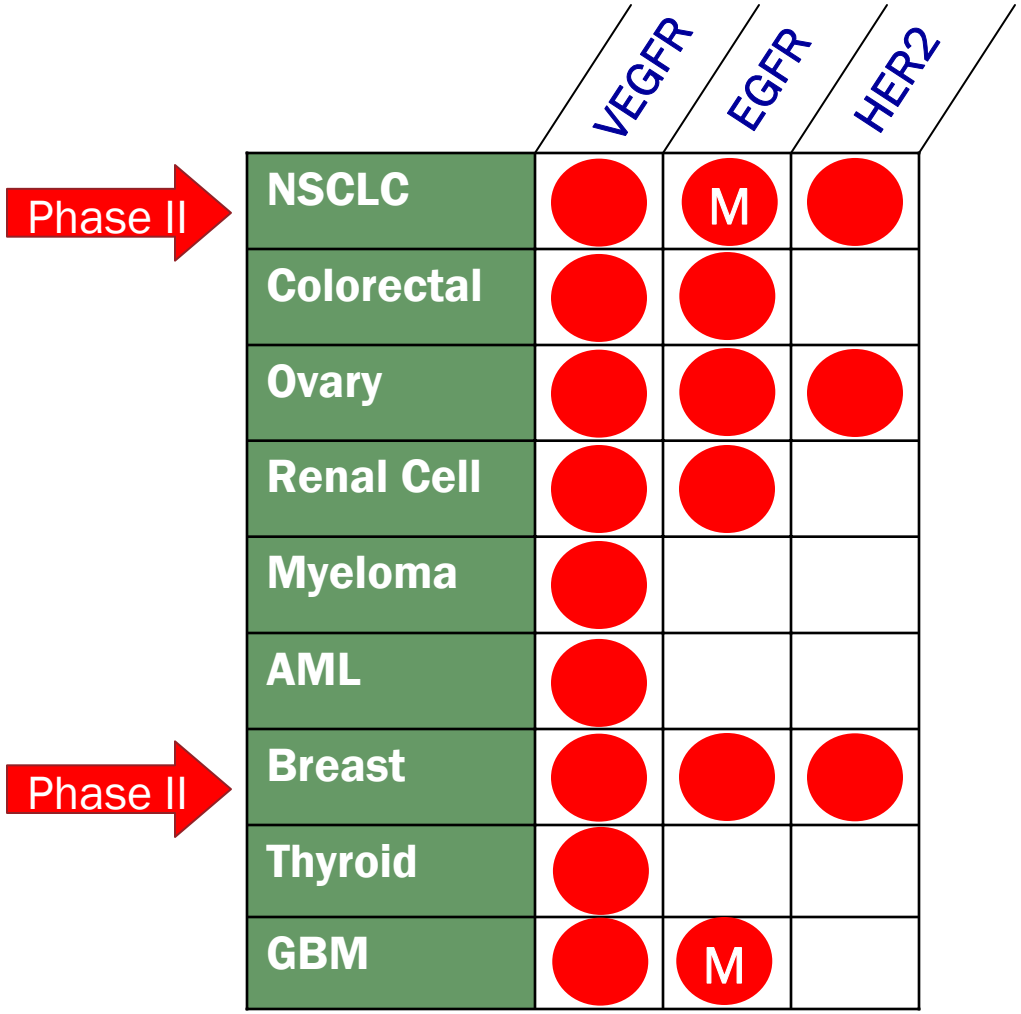
Gr. 2 rash reported at 4.68 mg/kg dose

Accrual ongoing to establish MTD

Phase II clinical program to proceed in Breast, NSCLC

Data Presented at EORTC-AACR-NCI Meeting, November 2005

XL647 – Potential Development Profile



A Phase II Study of XL647 in Subjects with Metastatic Breast Cancer

Target Population	Patients with metastatic breast cancer who have received prior anthracycline and taxane therapy
Study Design	Phase II non-randomized, open label
Objectives	Primary: determine confirmed response rate; evaluate safety and tolerability of 5d on 9d off schedule for 8 wks Secondary: determine PFS, OS, Duration of Response; further characterize PK and PD
Dose/route/regimen	Oral 350 mg/day; 5d on 9d off for 8 weeks; daily
Number of Subjects	Two-stage design; 17 patients initially enrolled, if ≥1 response, enroll total of 40 patients
Study Length	15 months for patient accrual and treatment
Assessments	Efficacy: at baseline and every 8 weeks; responses confirmed at approximately 30 days

A Phase II Study of XL647 in Subjects with Metastatic Non-small Cell Lung Cancer

Target Population	Patients with metastatic non-small cell lung cancer who have received no prior cytotoxic therapy
Study Design	Phase II non-randomized, open label
Objectives	Primary: determine confirmed response rate; evaluate safety and tolerability Secondary: determine PFS, OS, Duration of Response; further characterize PK and PD
Dose/route/regimen	Oral 350 mg/day; 5d on 9d off for 8 weeks; daily
Number of Subjects	Two-stage design; 19 patients initially enrolled, if ≥1 response, enroll total of 42 patients
Study Length	15 months for patient accrual and treatment
Assessments	Efficacy: at baseline and every 8 weeks; responses confirmed at approximately 30 days

A Phase II Study of XL647 in Subjects with Metastatic Non-small Cell Lung Cancer

Target Population	Patients with metastatic non-small cell lung cancer who have previously responded to Tarceva and progressed
Study Design	Phase II non-randomized, open label
Objectives	Primary: determine confirmed response rate; evaluate safety and tolerability Secondary: determine PFS, OS, Duration of Response; further characterize PK and PD
Dose/route/regimen	Daily
Assessments	Efficacy: at baseline and every 8 weeks; responses

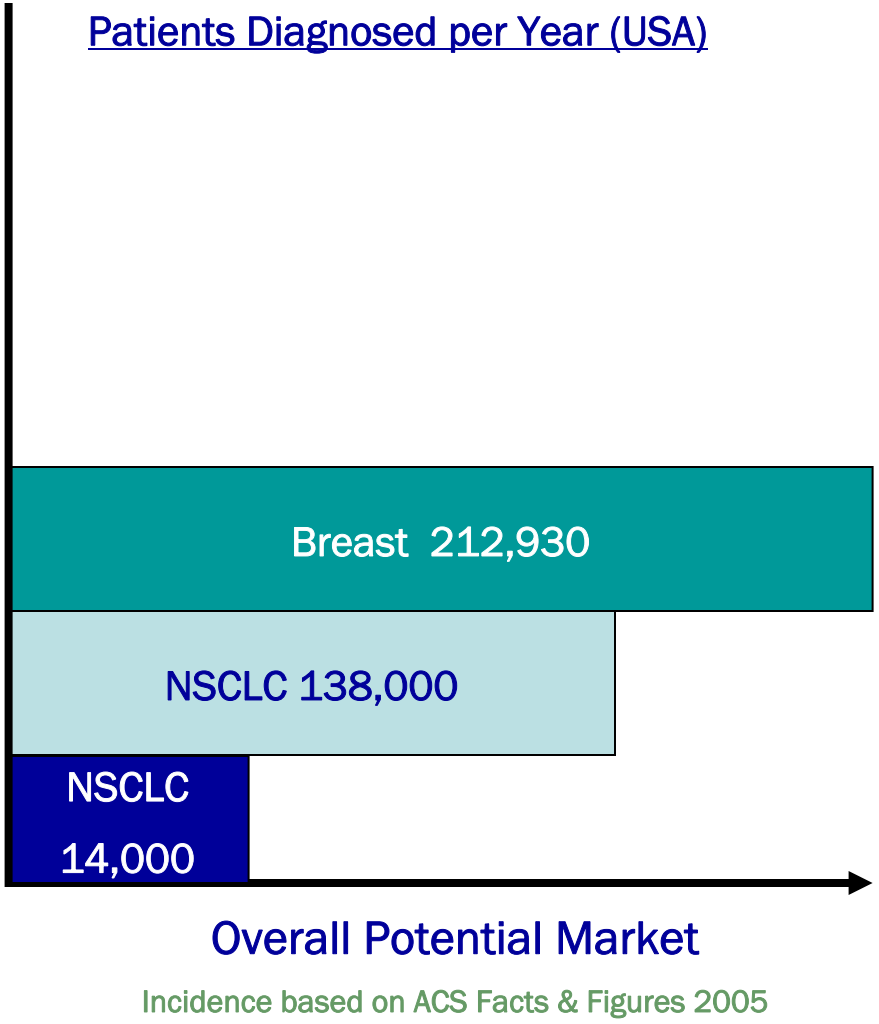
XL647: Market Entry and Expansion

Early Market Entry Point

- Previously responsive EGFR tumors which become resistant

Market Expansion

- VEGFR, HER2, EGFR
- Targets are validated or becoming validated in prevalent tumor types:
  - NSCLC, MBC



Incidence based on ACS Facts & Figures 2005

XL880 Rationale: c-Met & HGF in Cancer

c-Met and HGF are key drivers of tumor cell growth, motility, invasion, metastasis and angiogenesis

- Cell lines that ectopically overexpress c-Met become tumorigenic and metastatic in nude mice
- Transgenic expression in mouse models leads to malignant/metastatic lesions
- c-Met and HGF are frequently overexpressed in human tumors (carcinomas, sarcomas and hematopoietic malignancies)
- Activating c-Met mutations found in hereditary papillary renal carcinomas (HPRC): 8 distinct mutations described
- Activating mutations also found in sporadic tumors (some identical to mutations found in HPRC)

c-MET Mutation and Overexpression in Cancer

Tumor Type	Overexpression	Mutation	Comment
HPRC	Yes	100%	Familial
RCC	Yes	<10%	Inhibitor of HGF activation silenced (40%)
H&N	Yes	16%	Overexpressed in 70%of tumors
NSCLC	Yes	7%	HGF levels correlate with shortened survival
SCLC	Yes	12%	Coexpressed with c-Kit
Mesothelioma	Yes	?	HGF overexpressed
Glioblastoma	Yes	0	HGF overexpressed
Multiple Myeloma	Yes	0	HGF overexpressed
Breast	Yes	-	Poor prognosis

XL880 Summary

First in class c-Met inhibitor

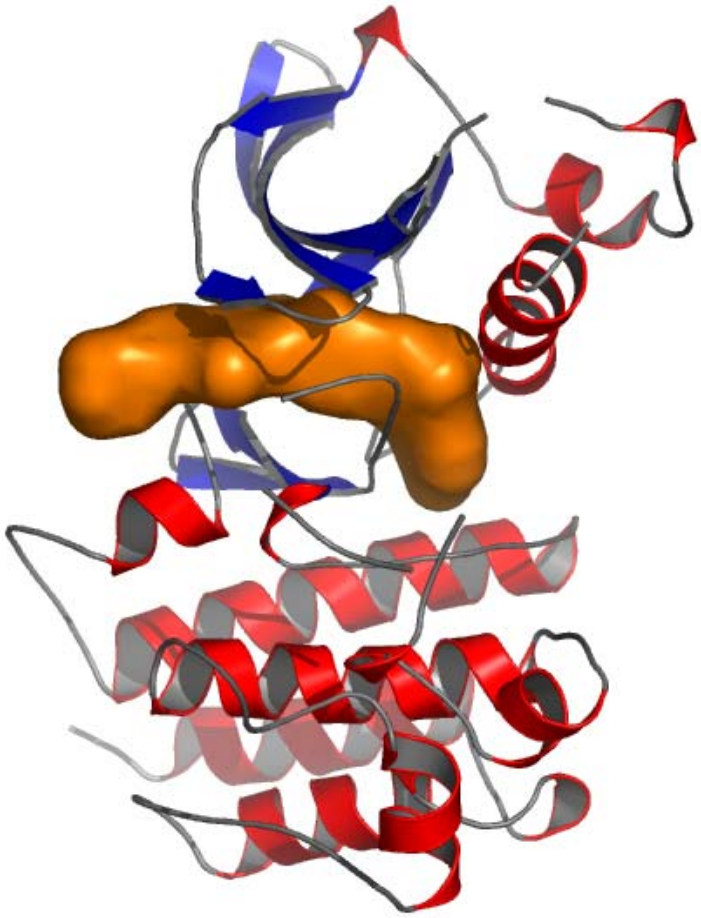
- sub-nM inhibition of c-Met and VEGFR2
- Slow off-rate ($t_{1/2}$>15 hours)

Excellent drug metabolism and pharmacokinetics properties

- High oral bioavailability
- >30 mg/ml solubility

Potent oral activity in multiple xenograft models

- Regression of large tumors
- Intermittent/single dose efficacy
- 10-100-fold more potent than SU11248 & MLN518 in FLT3 leukemia model



XL880-001 – Study Design And Subjects

Phase I, nonrandomized, open-label, dose-finding study

Adults (aged ≥18 years) with:

- Histologically confirmed metastatic or unresectable solid tumors
- ECOG performance status ≤2
- Life expectancy >3 months
- Adequate hematologic, renal, and hepatic function

Intermittent dosing 5 days out of 14

- Oral dosing of XL880 as either an aqueous liquid formulation (all dose levels) or as a 20 mg capsule (0.4 mg/kg dose group)

XL880-001 – Adverse Events

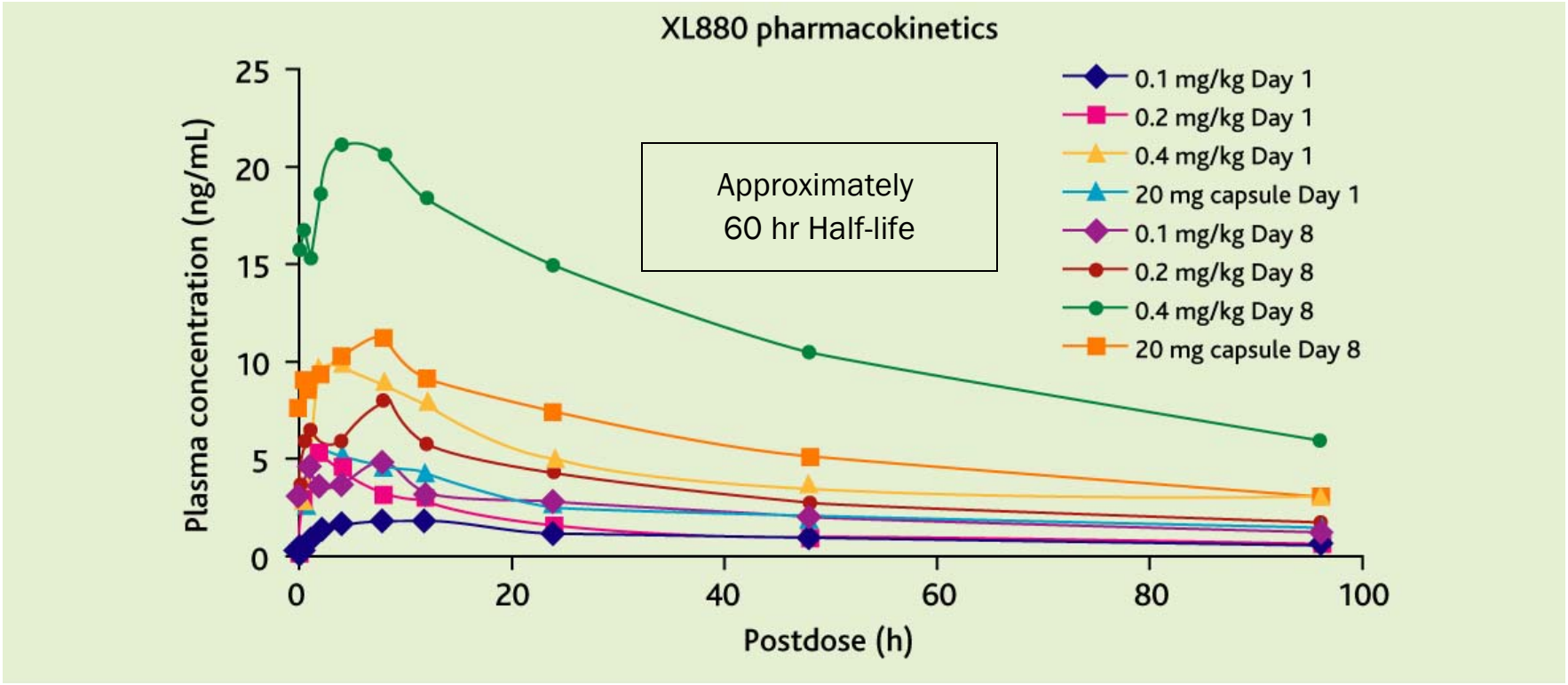
No treatment-related toxicities of any grade have been reported to date

The MTD has not yet been reached

Data Presented at EORTC-AACR-NCI Meeting, November 2005

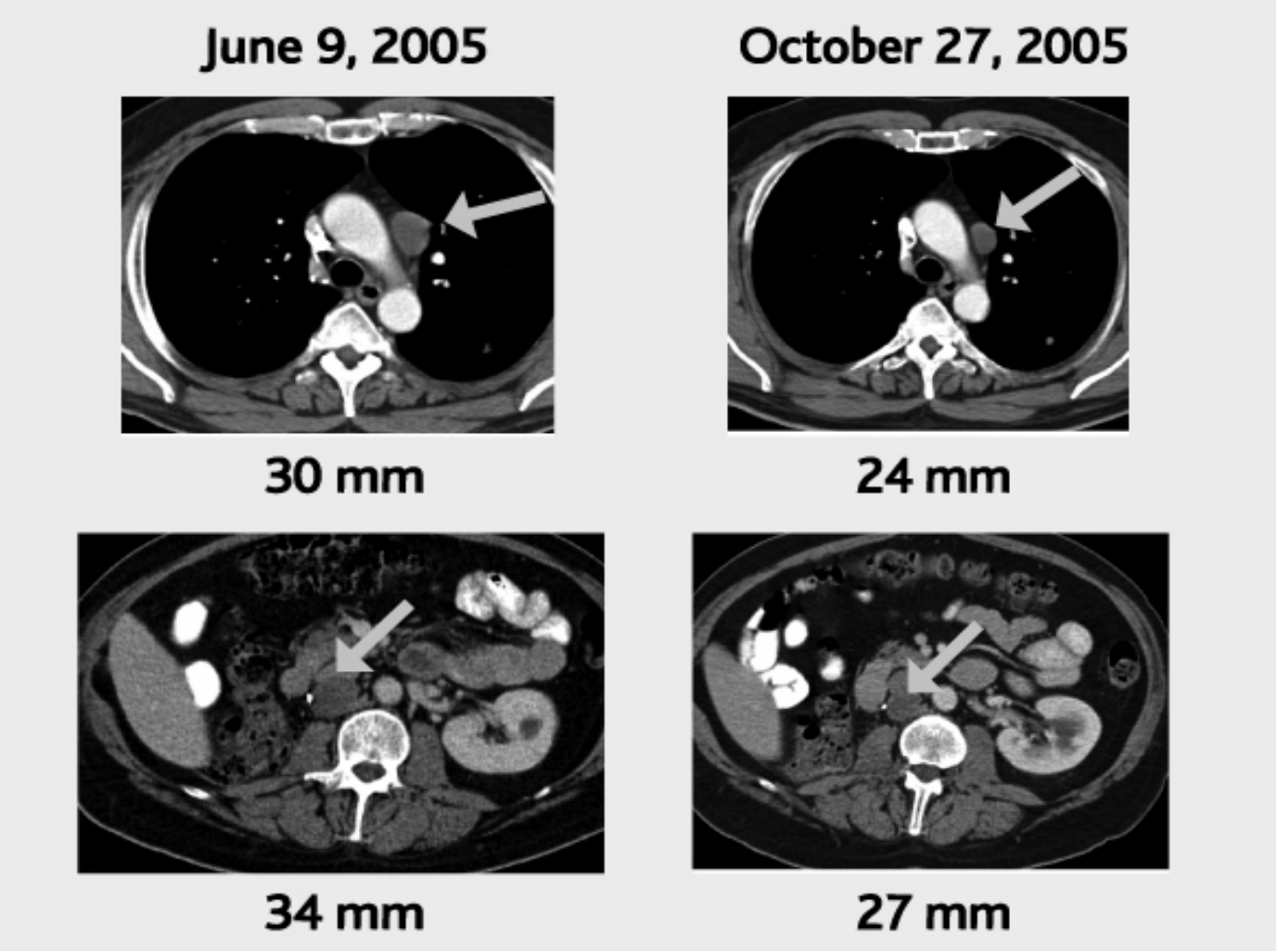
XL880-001 – Pharmacokinetics

Data represent group mean values (n=3 patients per group) following a single dose (Day 1) or 5 consecutive daily doses (Day 8)



Data Presented at EORTC-AACR-NCI Meeting, November 2005

XL880-001 – Clinical Efficacy



XL880-001 – Conclusions

XL880

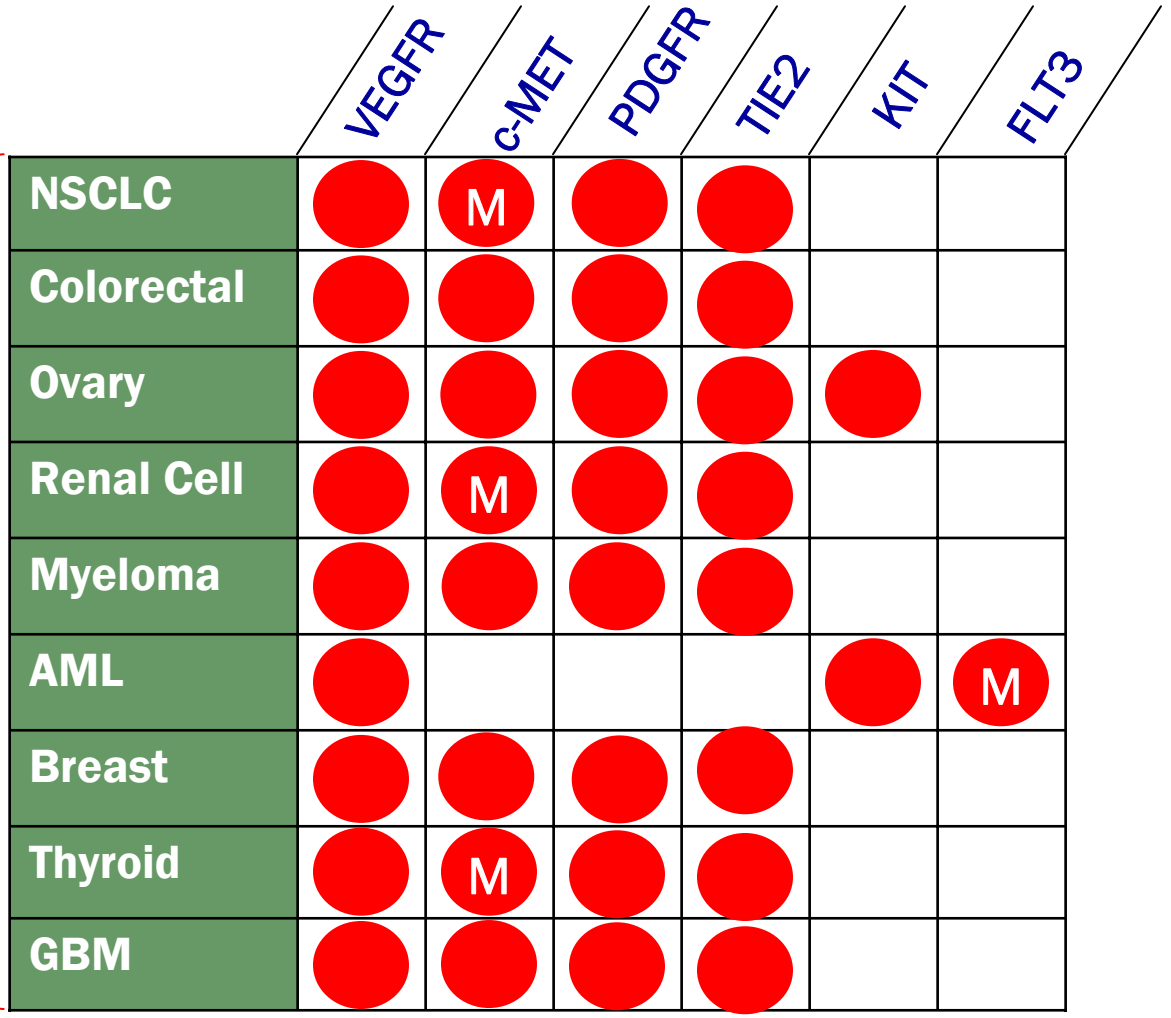
- RTK inhibitor with a novel spectrum of targets on both tumor cells and tumor-associated vasculature
- Substantial preclinical antitumor activity
- Well tolerated up to and including the 0.4 mg/kg dose level

The MTD has not yet been reached and dose escalation is ongoing

Data Presented at EORTC-AACR-NCI Meeting, November 2005

XL880 – Potential Development Profile

Multiple Phase II Trials Under Consideration for Initiation in 2006



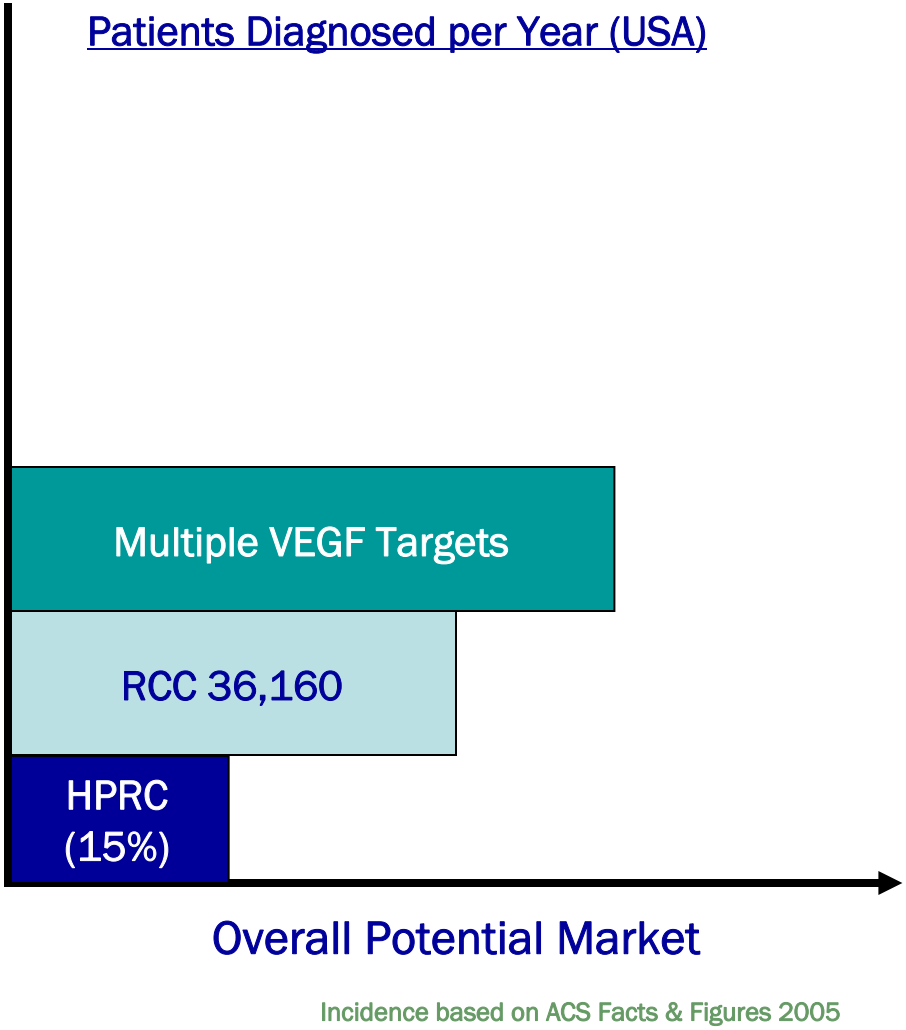
XL880: Market Entry and Expansion

1. Early Market Entry Point

- Hereditary Papillary Renal Cell: c-Met targeting

2. Market Expansion

- VEGFR
- In validated tumors



Incidence based on ACS Facts & Figures 2005

A Spectrum-Selective Protease Inhibitor

XL784 inhibits 2 mechanisms contributing to renal disease:

ADAM10: cleavage of membrane-bound TGF-α activates EGFR, which contributes to renal damage

MMP2: required for epithelial-mesenchymal transition (EMT) involved in renal pathobiology

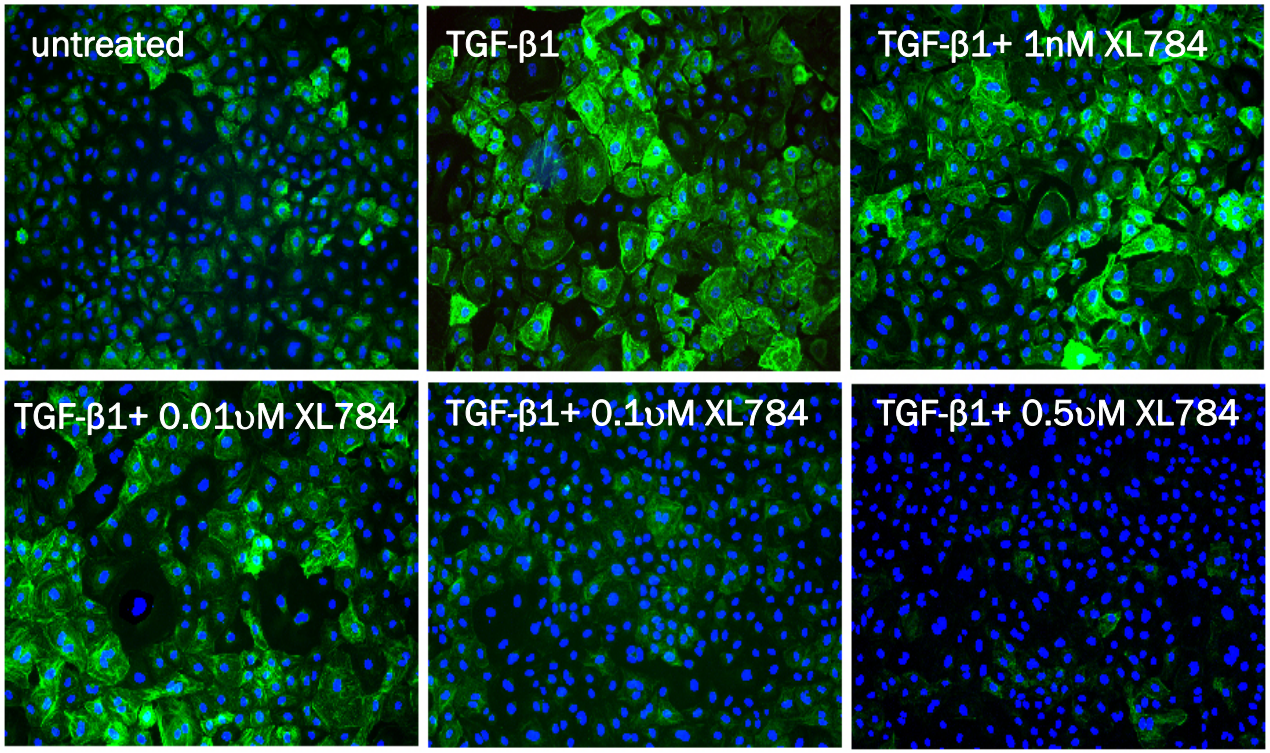
XL784 potently inhibits MMP2 activity (directly) and cleavage of TGF-α (via ADAM proteins)

Protease	XL784 IC_{50} (nM)
ADAM10	1.5
ADAM17 (TACE)	70
MMP1	2000
MMP2	0.8
MMP3	120
MMP8	11
MMP9	18
MMP13	0.56

XL784 in Chronic Renal Disease

MMP2: expressed in response to TGF-β, induces EMT:

Fibroblast recruitment → renal fibrosis → proteinuria & kidney failure



XL784 inhibits TGF-β-induced EMT in cultured rat renal epithelial cells

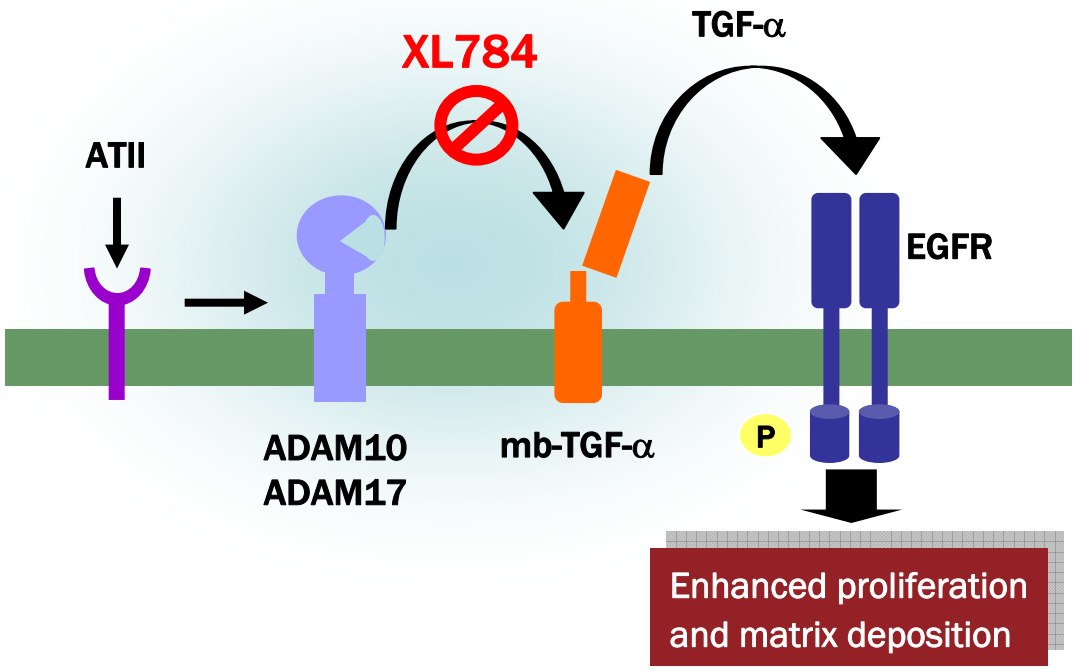
DAPI

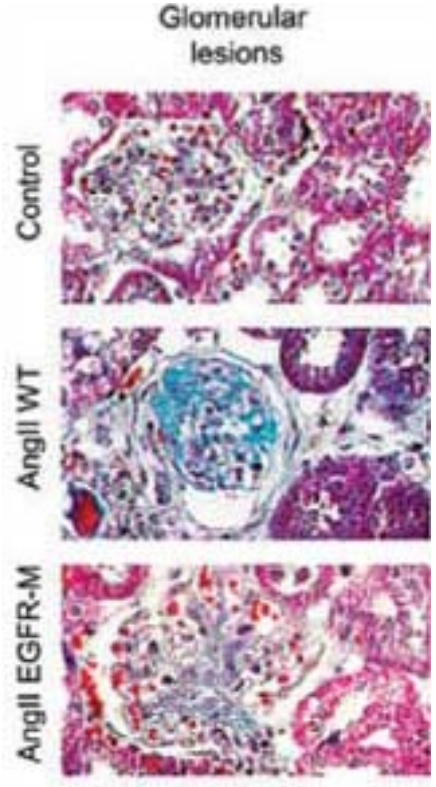
smooth muscle actin

XL784 in Chronic Renal Disease

ADAM Cleavage of membrane-bound TGF-α is required for development of renal lesions in response to ATII

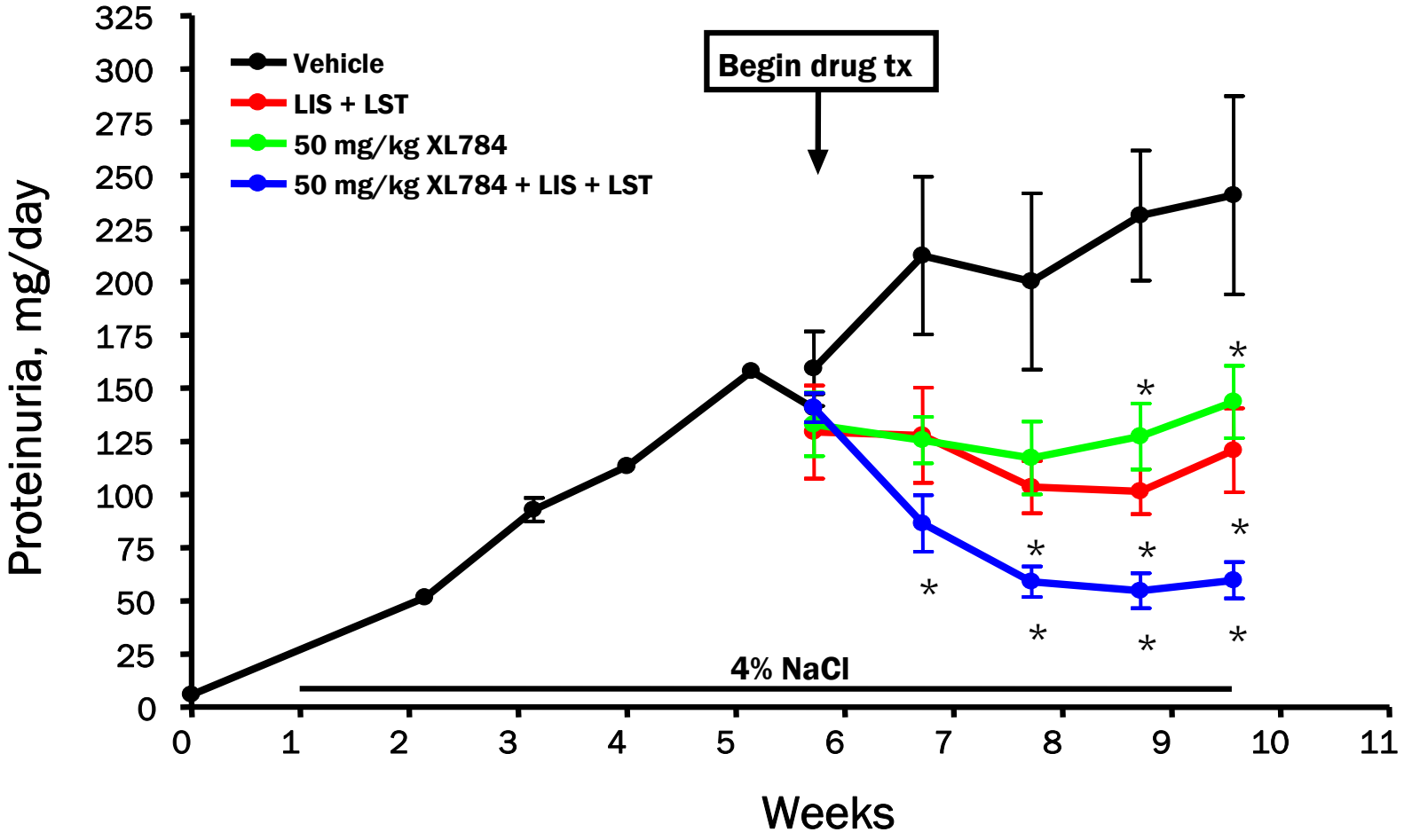
- Enhanced proteinuria and renal damage



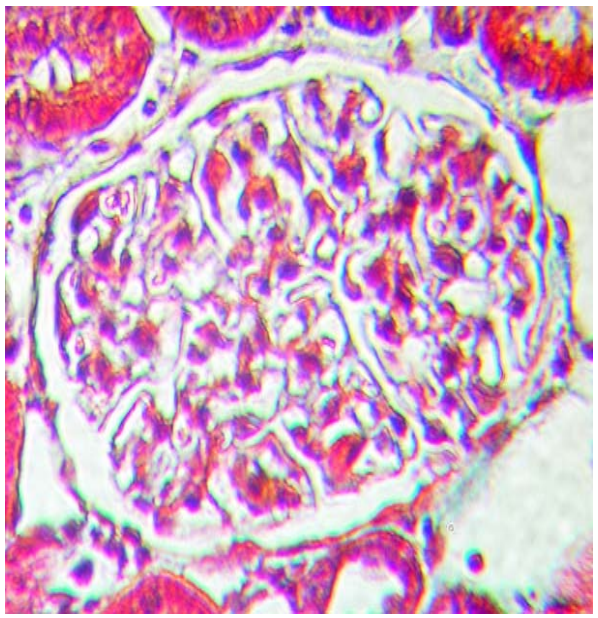


Lautrette et al
Nat Med Aug 05

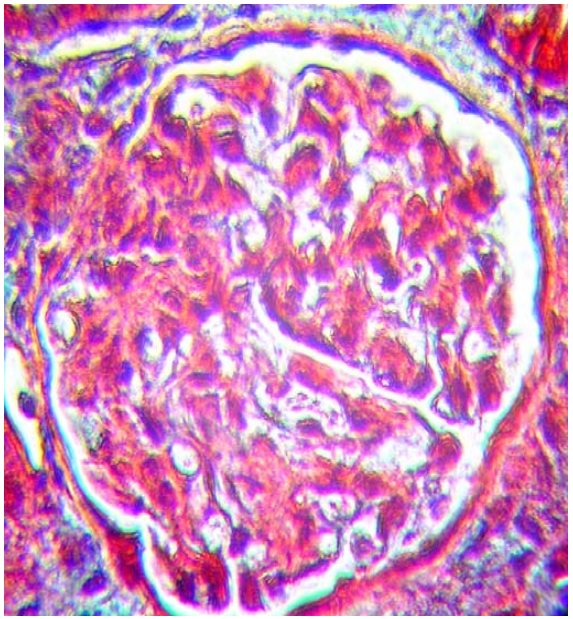
Effects of XL784 versus ACEI & ARB on Proteinuria in Dahl SS Rats



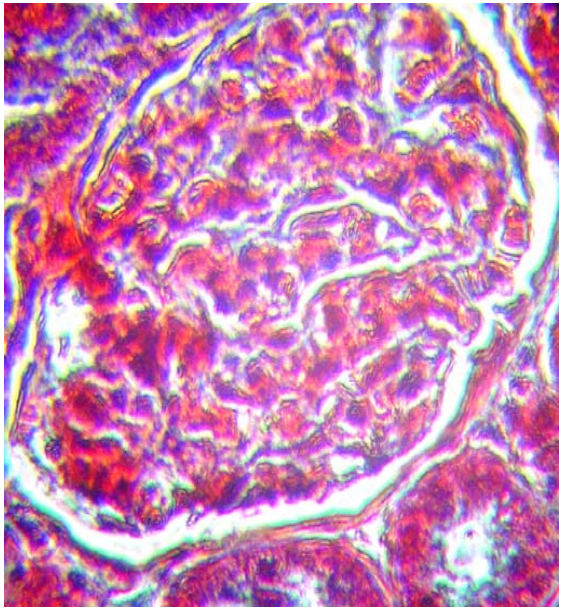
Effect of XL784 on Glomerular Injury in Dahl SS Rats



XL784

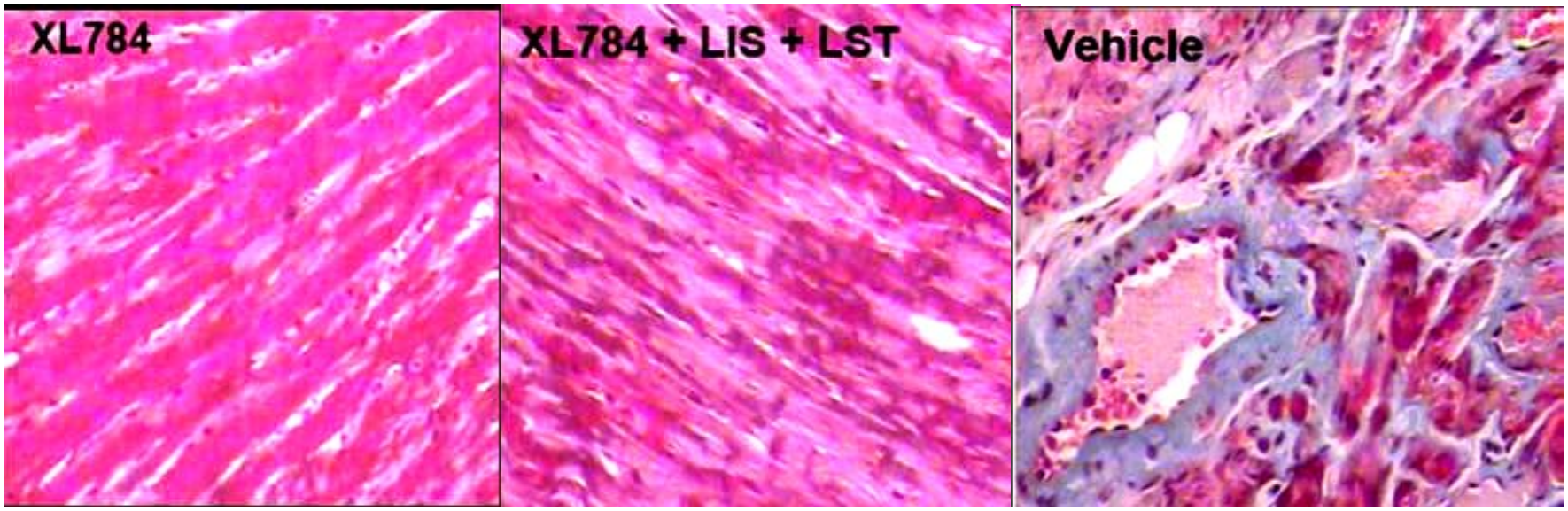


Lis+Lst



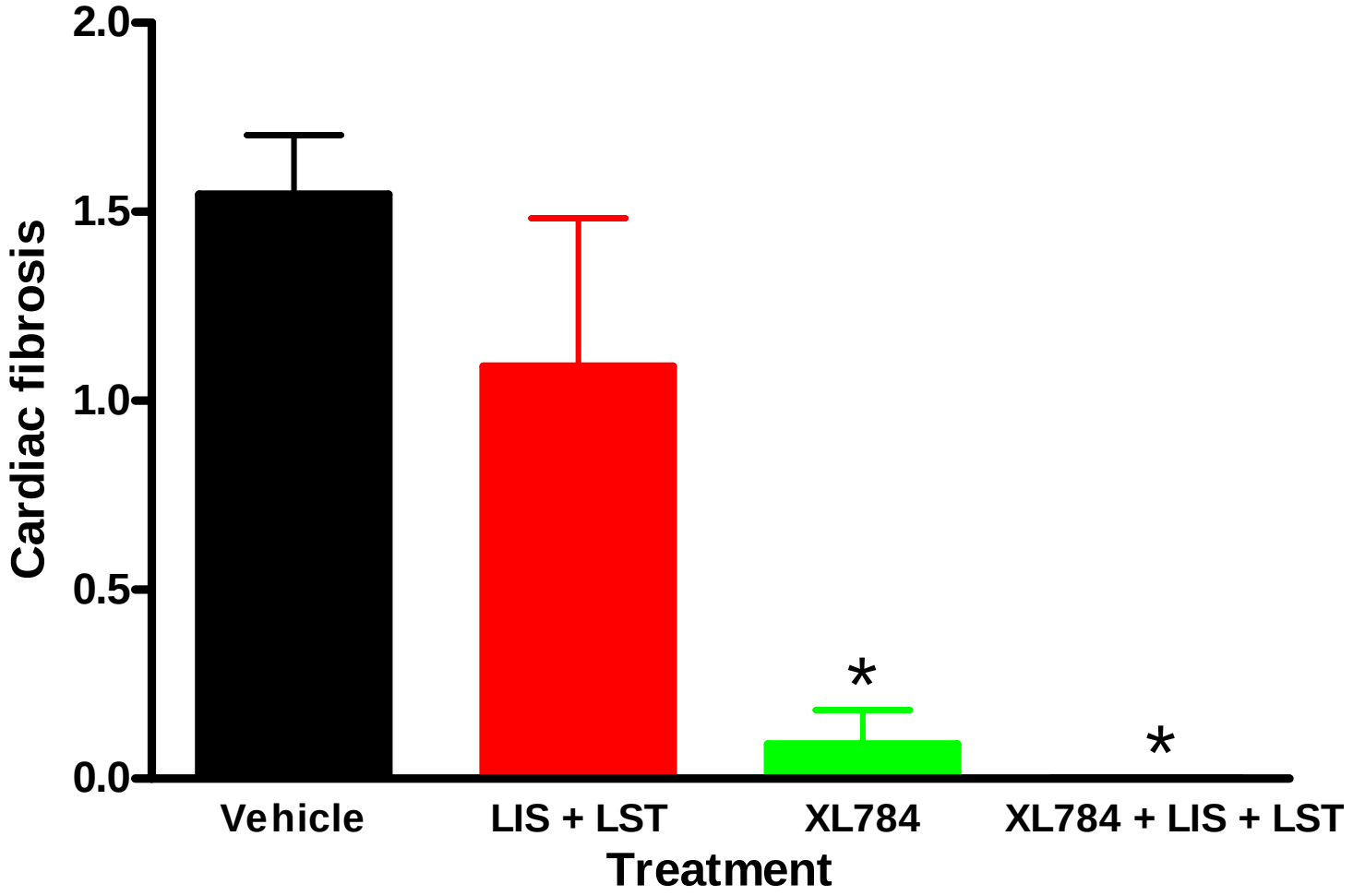
Vehicle

Effect Of XL784 On Cardiac Fibrosis In Dahl SS Rats



XL784 | XL784+Lis+Lst | Vehicle

Effect of XL784 versus AII blockade on cardiac fibrosis



Summary and Conclusion – Hypertensive Model

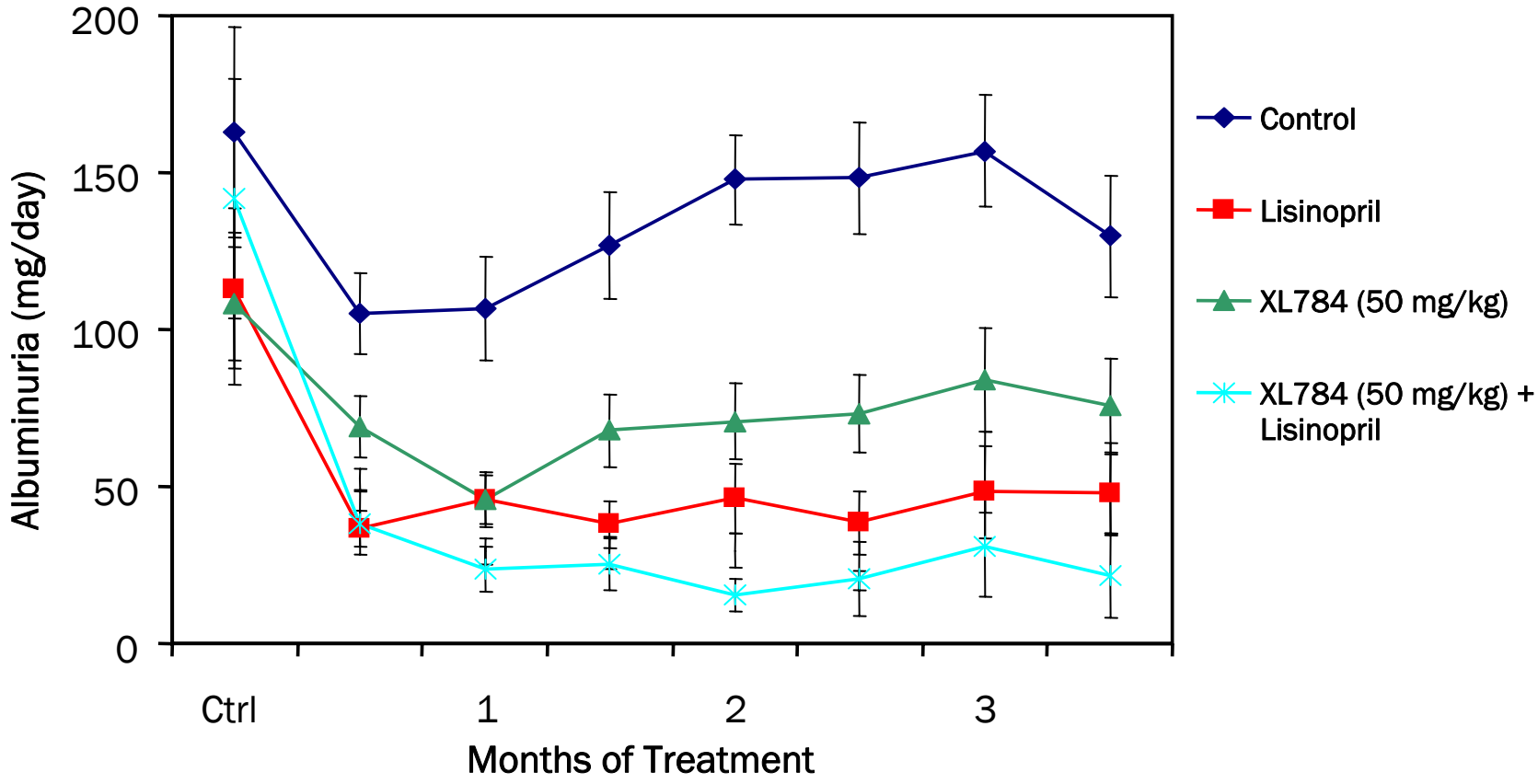
XL784 prevents the progression of proteinuria and glomerular injury in Dahl SS rats with established hypertension and preexisting renal disease without reducing mean arterial pressure. It is more effective than the combination of an ACE inhibitor and an AT1 blocker

XL784 moderately lowers serum cholesterol and triglycerides

XL784 in combination with lisinopril and losartan was more effective than the individual treatments. XL784 in combination with lisinopril and losartan shows potential for the reversal of hypertension-induced renal disease

XL784 completely inhibits cardiac fibrosis in animals with hypertension

Comparison of treatments on albuminuria in T2DN rats – A Model of Human Diabetic Nephropathy



XL784 – Conclusions

XL784 is well tolerated

Lowers plasma lipids

XL784 reduces proteinuria, slows the progression of hypertensive and diabetic nephropathy

The renal protective effects of XL784 are additive with effects of ACE and ARB therapy

XL784-001 – Single Dose Phase 1 Study

Design

- Single-blind design in healthy volunteers
- Sequential, between subjects, dose-escalation
- 8 subjects per dose level, randomly allocated to receive:
  - vehicle control (n=2) or XL784 (n=6)

Test article

- XL784 powder in bottle (corn oil vehicle)
- Doses (mg): 30, 60, 120, 240, 450, 750, 1000, 1300, 1700

Outcome measures

- Clinical signs and symptoms
- Clinical laboratory, EKG
- Plasma samples for determination of drug concentration

XL784-001 – Single-dose Phase 1 Results

Well tolerated to maximum dose of 1.7grams/subject

- No drug-related adverse effects

Pharmacokinetic Profile

- Orally bioavailable
- Dose-proportional exposure
- Linear pharmacokinetics with ~8 hour elimination half-life

XL784-102 – Repeat-Dose Phase 1 Study

Healthy Volunteers

Double-blind, placebo controlled

Daily administration for 2 weeks

- Cohort A: 100 mg/day, n=18 (12 active, 6 placebo)
- Cohort B: 200 mg/day n=18 (12 active, 6 placebo)

Objectives

- Tolerability
- Pharmacokinetics
- First human trial of novel solid oral dosage form
- Drug metabolism effects
  - Alprazolam PK pre- and post- XL784
- Pharmacodynamics

XL784-002 – Repeat Dose Phase 1 Preliminary Data

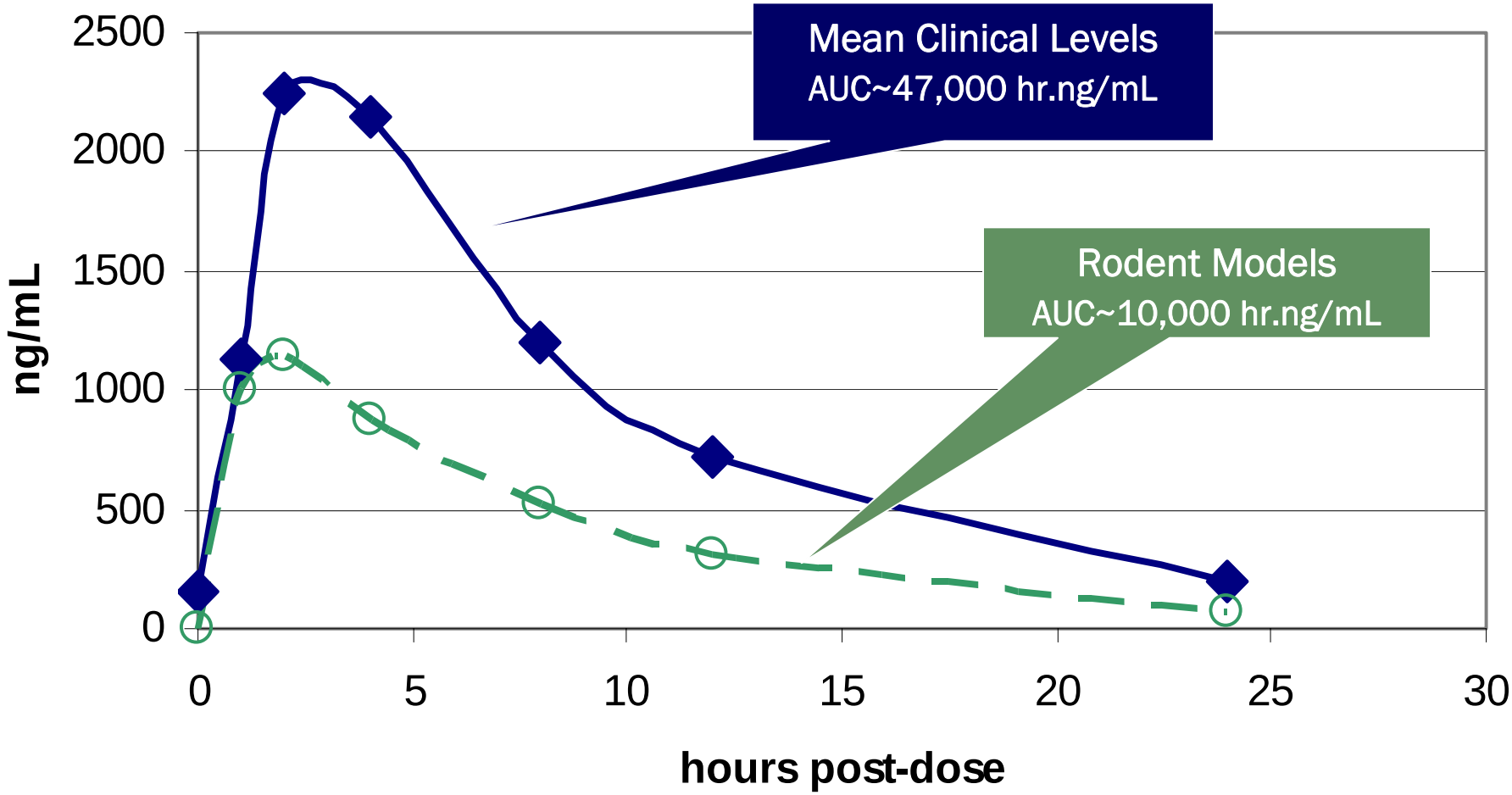
Well tolerated

- No drug-related adverse effects

Target Pharmacokinetic Exposure Achieved

Analysis of PD endpoints ongoing

XL784 Relative Exposure



XL784 – Drug Interaction Potential

In pre-clinical studies, XL784 interacted with the CYP450 Isozyme 3A4

The repeat dose Phase 1 study included administration of alprazolam (known to be metabolized via 3A4) as a probe for interaction potential

XL784 appeared to induce the CYP450 Isozyme 3A4

- In healthy volunteers, XL784 @ 200 mg daily for 14 days increased alprazolam clearance approximately 50%

Known 3A4 Substrates

- Carbamazepine, diltiazem, erythromycin, itraconazole, ketoconazole, ritonavir, atorvastatin, simvastatin, theophylline, verapamil, warfarin

Efficacy of known 3A4 substrates may be reduced by concurrent treatment with XL784

- Will include cautionary information in Phase 2 protocol and IB

XL784 – Phase 2 Clinical Trial Concept

Patients with Type II diabetes and proteinuria

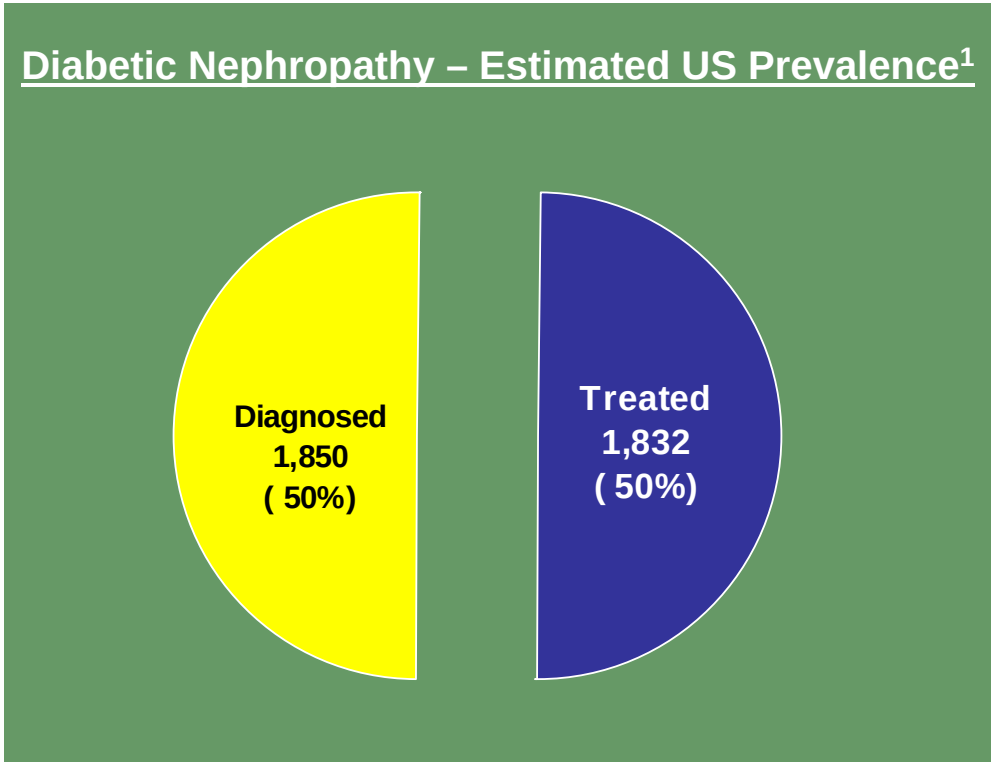
- Optimal control of diabetes
- Optimal control of blood pressure
  - On stable treatment with ACE or ARB
- Clinically significant proteinuria
- Moderate renal impairment

Randomly allocate to receive XL784 (200 mg daily) or identical placebo capsules

- Primary endpoint = reduction in proteinuria
  - Based on Albumin / Creatinine Ratio
- Secondary endpoints
  - Change in renal function
  - Cardiovascular events (MI, stroke, death)
- Time on study 3 months
- Sample size ~ 130 patients

Target start in early 2006

XL784 – Diabetic Nephropathy Market Opportunity



Market Opportunity

Estimated that each year there are 3.7 million patients living with diabetic nephropathy in the US[1]

Approximately 1.85 million patients are diagnosed and treated annually[1]

Best-in-class potential

Decision Resources, October 2004

Charting Our Own Course
The First Annual Exelixis R&D Day

EXELIXIS™

BREAK

New Targets, New Opportunities

XL184: Rationale

XL184: A structurally distinct compound which retunes key in vitro and in vivo profile of XL880

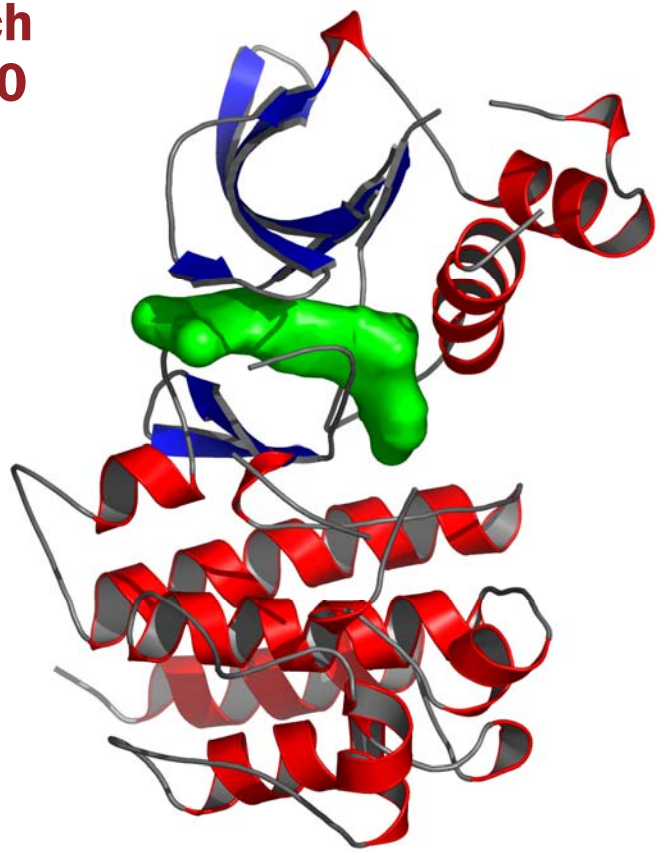
- Best-in-class VEGFR2 inhibitor with 35 pM activity
- Low nM activity vs. c-Met, TIE2, KIT

XL184 has excellent pharmacokinetic properties

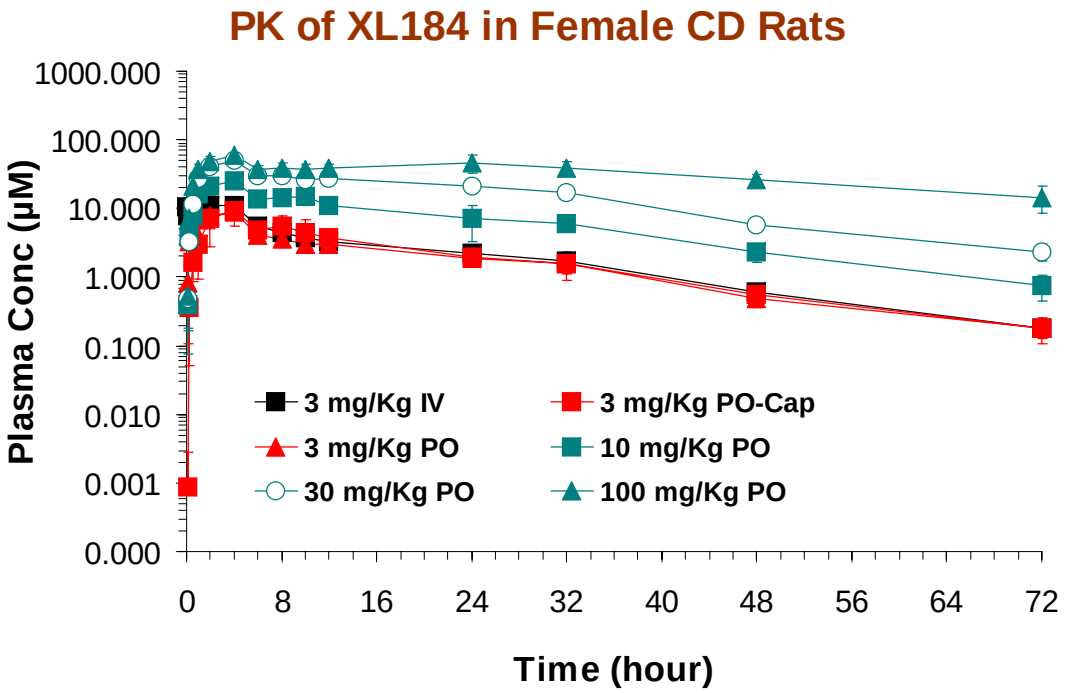
- High exposure and excellent bioavailability

Extremely potent & efficacious in xenograft models

- Potent anti-tumor activity in broad array of tumor xenografts
- Single dose efficacy
- Excellent tolerability in preclinical models

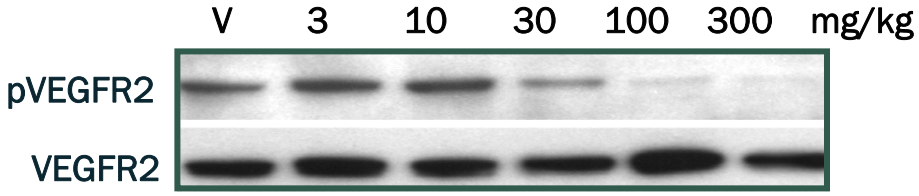


Pharmacokinetics and Pharmacodynamics

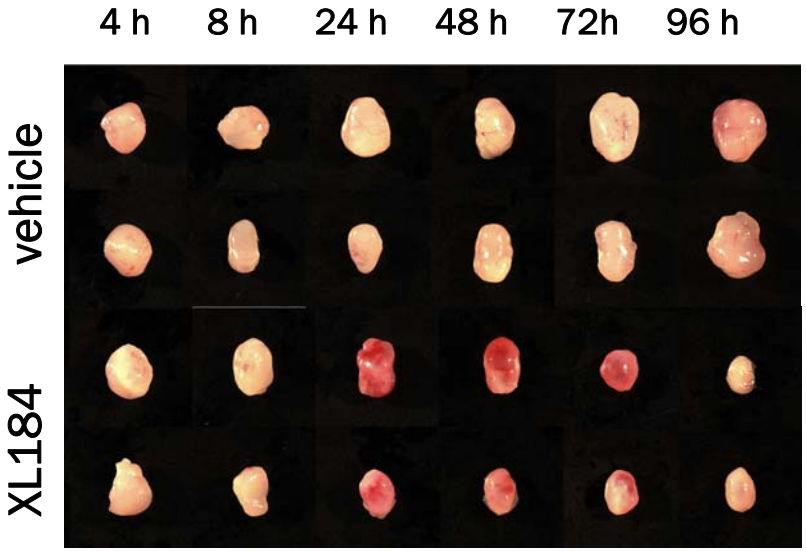


Long duration of action, high oral bioavailability

In vivo modulation of VEGFR2 activity

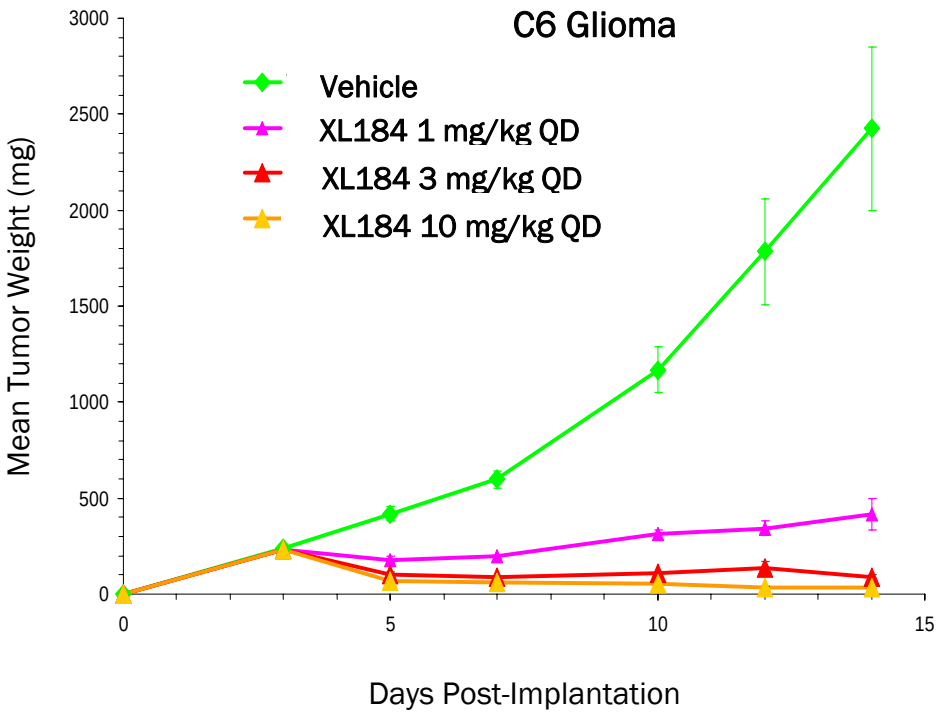


XL184 in vivo Efficacy



Rapid onset of tumor surface hemorrhage

Phase 1 in progress



Potent anti-tumor activity at well-tolerated doses

XL820 Summary

Potent inhibitor of wt & mutant KIT RTKs

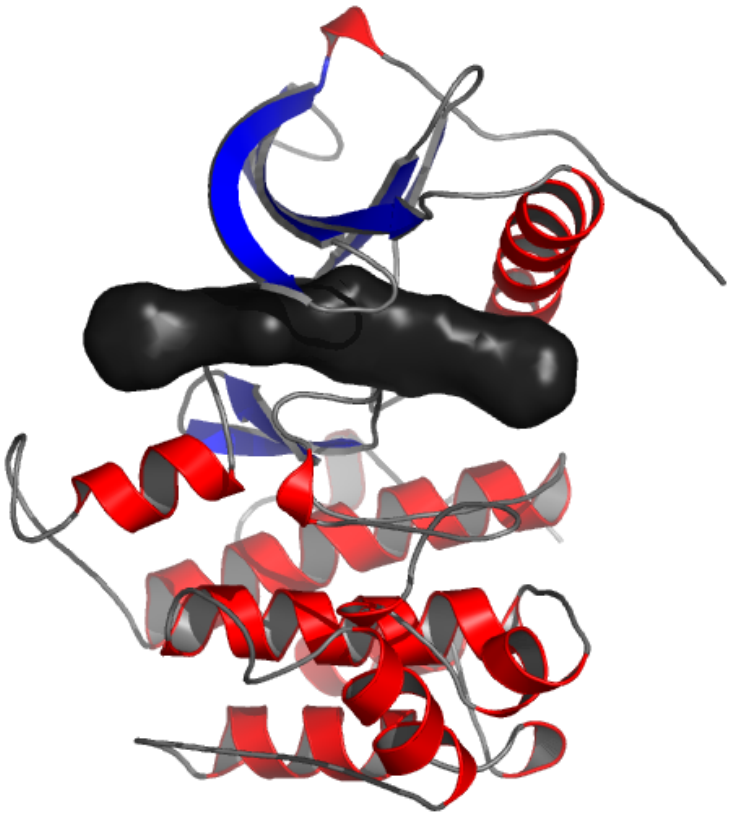
- Also inhibits VEGFR2, FLT3 and PDGFR

Potent PD & anti-tumor activity at well-tolerated doses

- Excellent oral bioavailability and pharmacokinetics

XL820 is a novel SS-RTK ideally tuned for GIST, SCLC & AML

- KIT activating mutations and overexpressed wt-KIT drive proliferative phenotype



XL820: In vitro Activity

Kinase	IC_{50} (nM)
KIT	9
Flt3	64
PDGFR-α	9
PDGFR-β	35
KDR	6

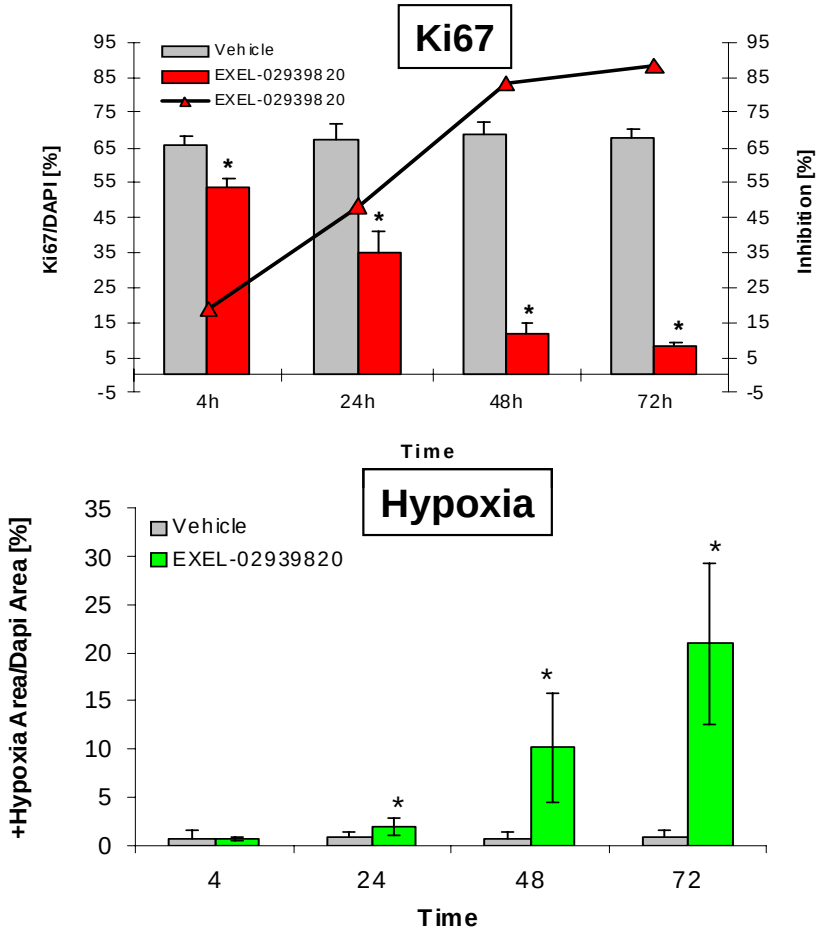
RTK	IC_{50} (nM) Autophosphorylation
KIT	9
KDR	17
Flt3	48

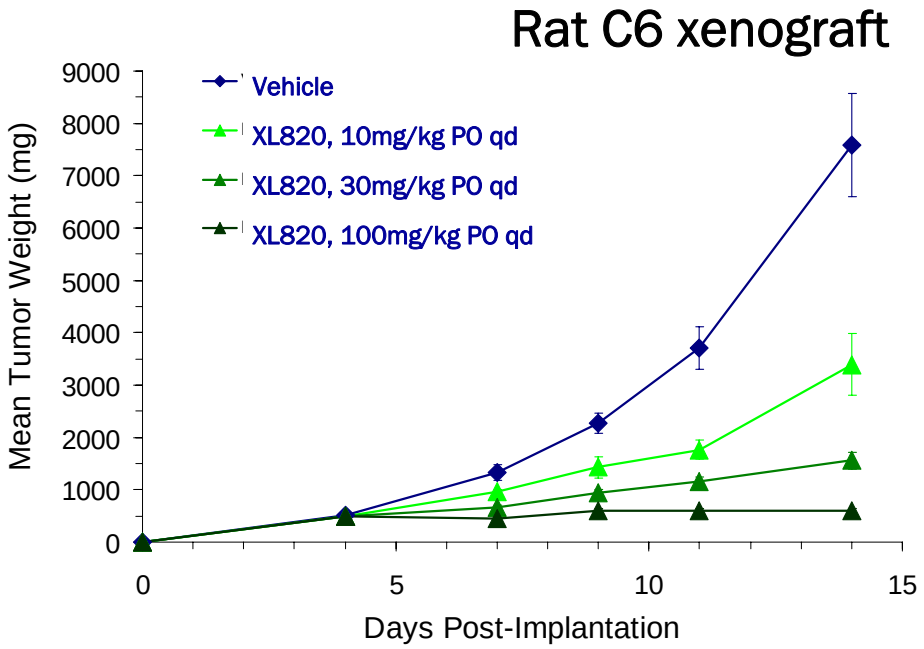
Compound	Cellular Autophosphorylation IC_{50} (nM)		
	KIT (WT)	KIT (JMD)	KIT (YKD)
XL820	9	0.5	26
Gleevec	430	8.7	250
SU11248	7	11	38

High potency against wild-type and mutationally-activated forms of KIT

Evaluation of additional KIT mutants in progress:
T670I, V654A, D816V, D820V, N822K

XL820: In vivo Activity





XL820 Impacts tumor cell growth & vessel density/hypoxia

Phase 1 in progress

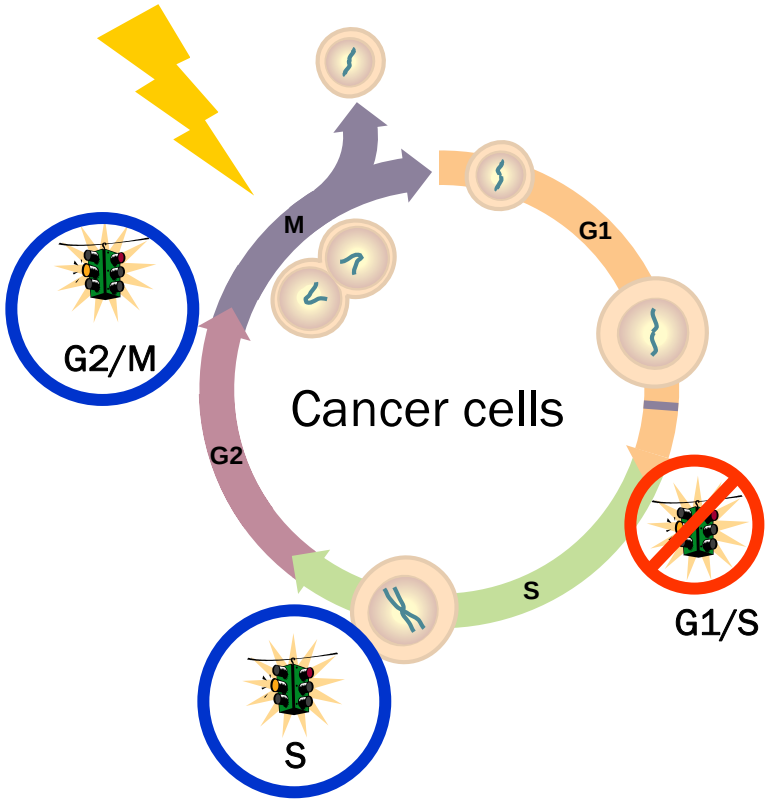
XL844 Rationale: Checkpoint Inhibition

Cells halt progression through cell cycle in response to DNA damage

- chemotherapy
- radiation
- limits efficacy

Chk kinases are key components of the DNA damage response pathway

- inhibition abrogates cell cycle arrest
- cell cycle continues with damaged DNA
- results in cell death



XL844 – Summary

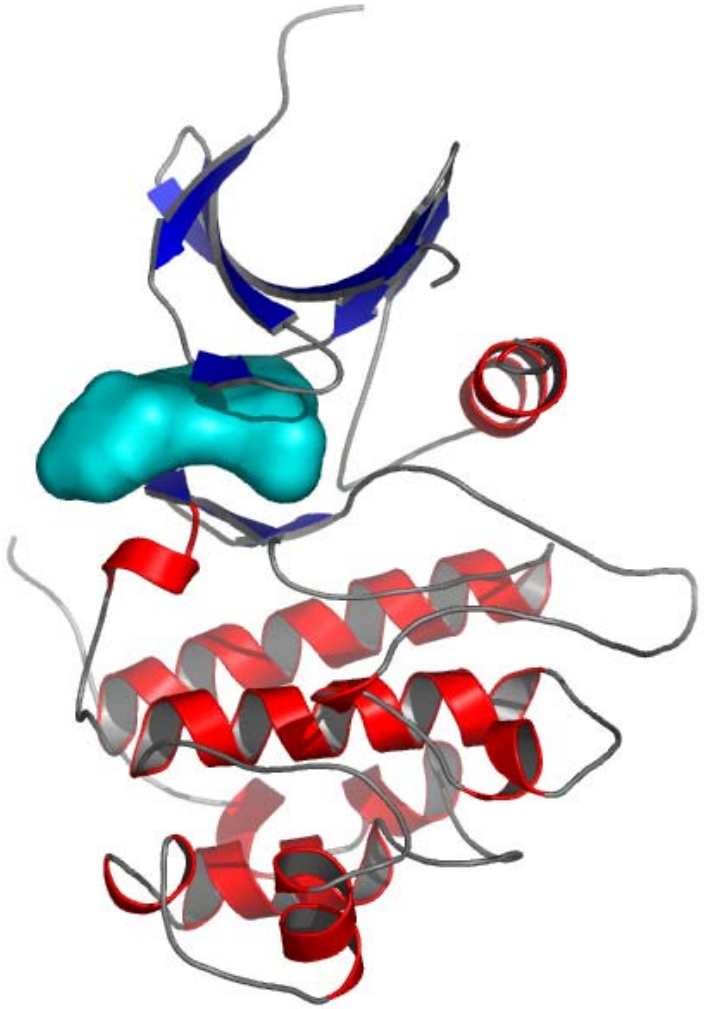
Potent inhibitor of Chk1 and Chk2 kinases

Abrogates DNA-damage checkpoints in vitro and in vivo

High aqueous solubility, metabolic stability, PK and tolerability

Synergistically potentiates activity of genotoxic agents

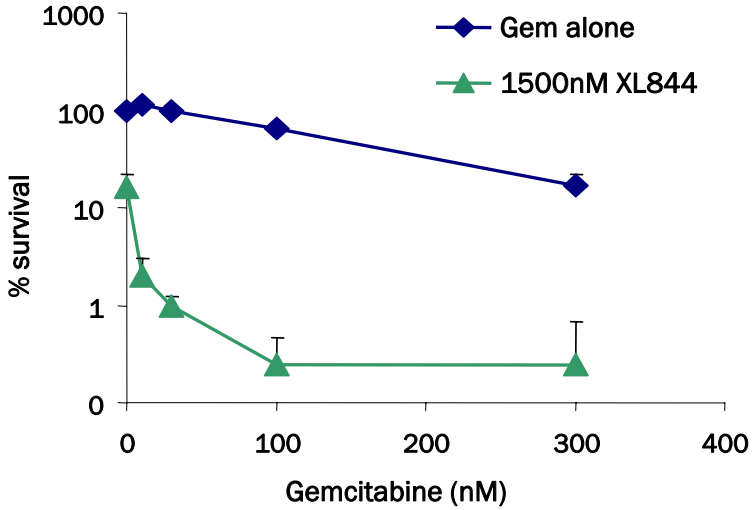
First specific Chk1/Chk2 inhibitor to advance into the clinic

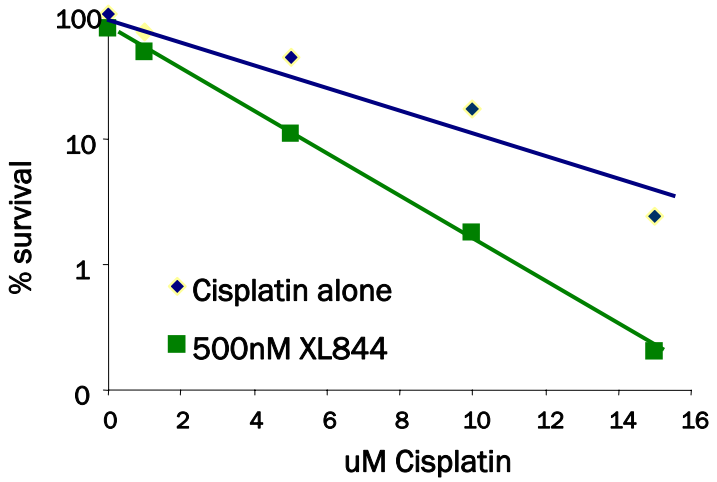


XL844: In vitro Activity

Kinase	IC_{50} (nM)
Chk1	2.2
Chk2	0.22
Flt-4	6
KDR	12
PDGFR-β	25
Flt-3	28

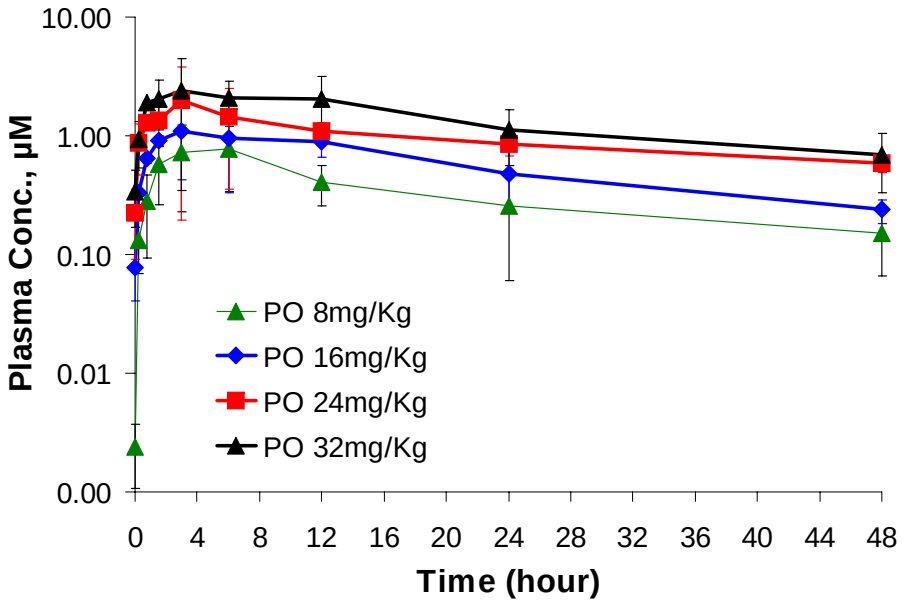
Potentiation of DNA damaging agents by XL844

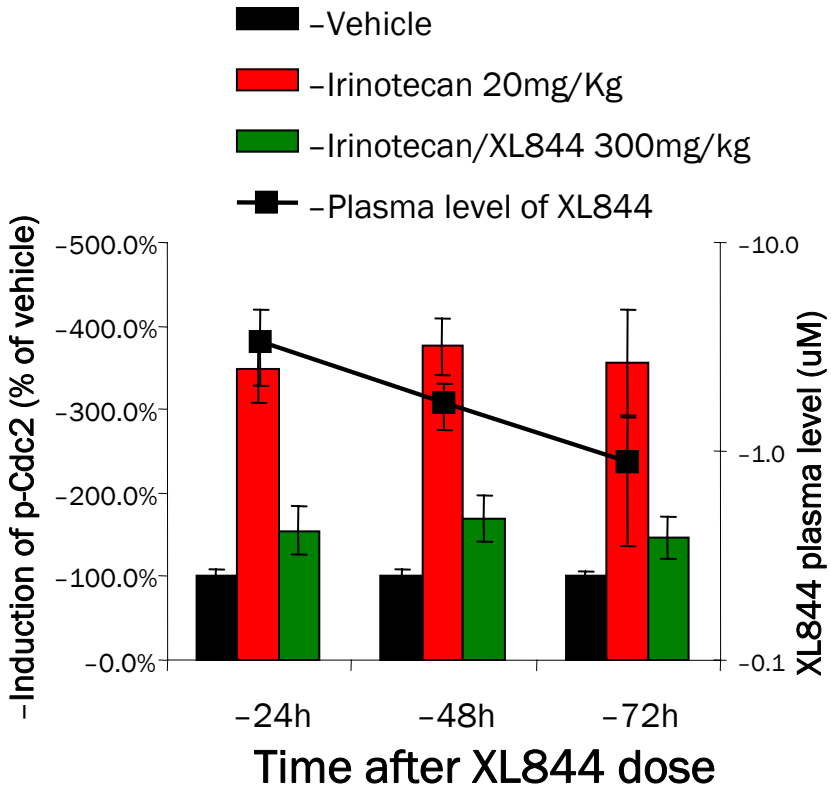




XL844 – Pharmacokinetics and Pharmacodynamics

PK of XL844 in Male Beagle Dogs

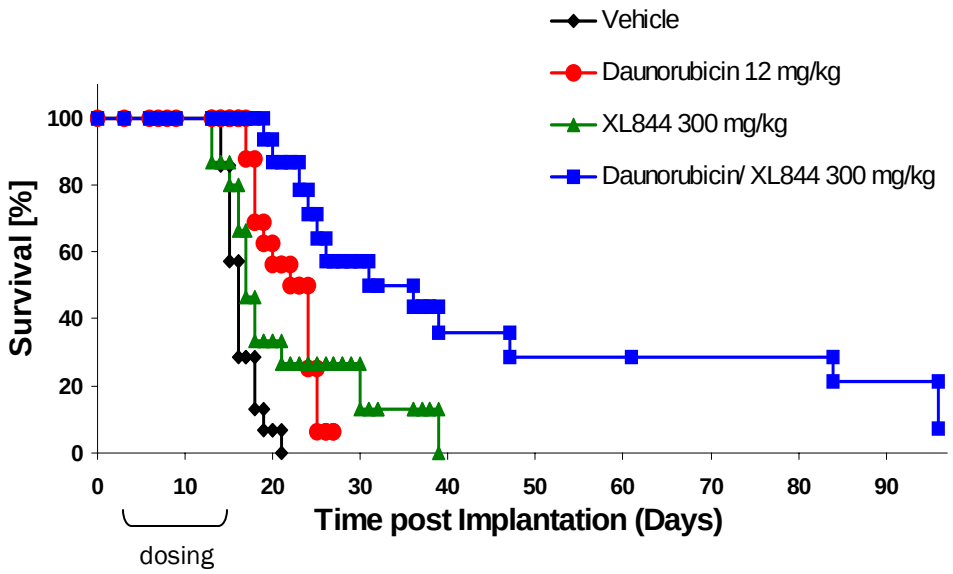




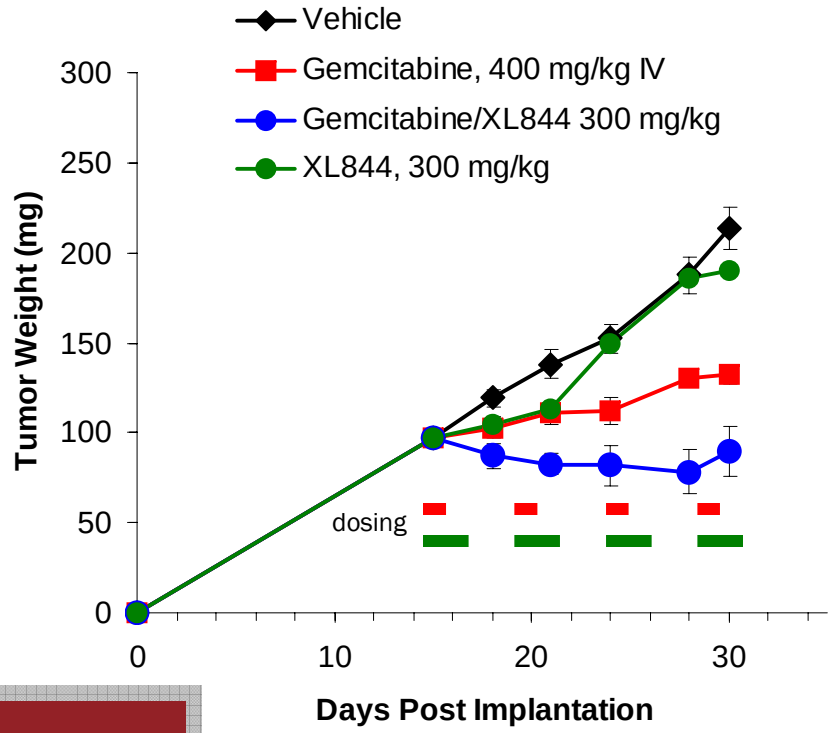
Good pharmacokinetic profile
Long pharmacodynamic duration of action

XL844 Efficacy

Long term potentiation of survival in K562 CML model



Potentiation of Gemcitabine in Panc-1 pancreatic carcinoma model



Phase 1 in progress

XL228: Summary

Potent dual inhibitor of IGF1R & SRC

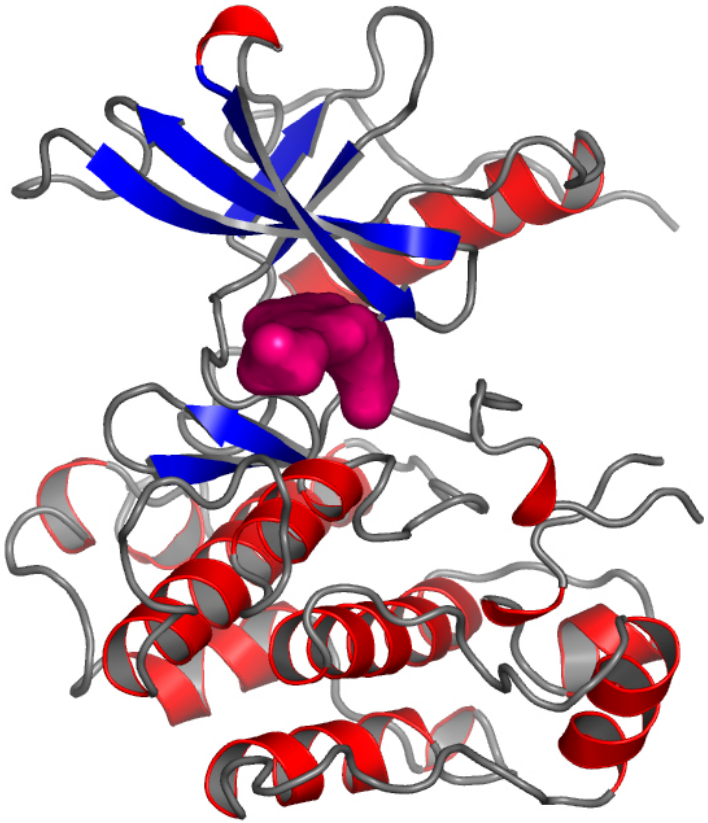
- IGF1R enhances cell growth and survival
- SRC cooperates with FAK to promote motility and invasion

Potent inhibitor of wt & mutant Abl

- Effective against Gleevec and dasatinib resistance mutations

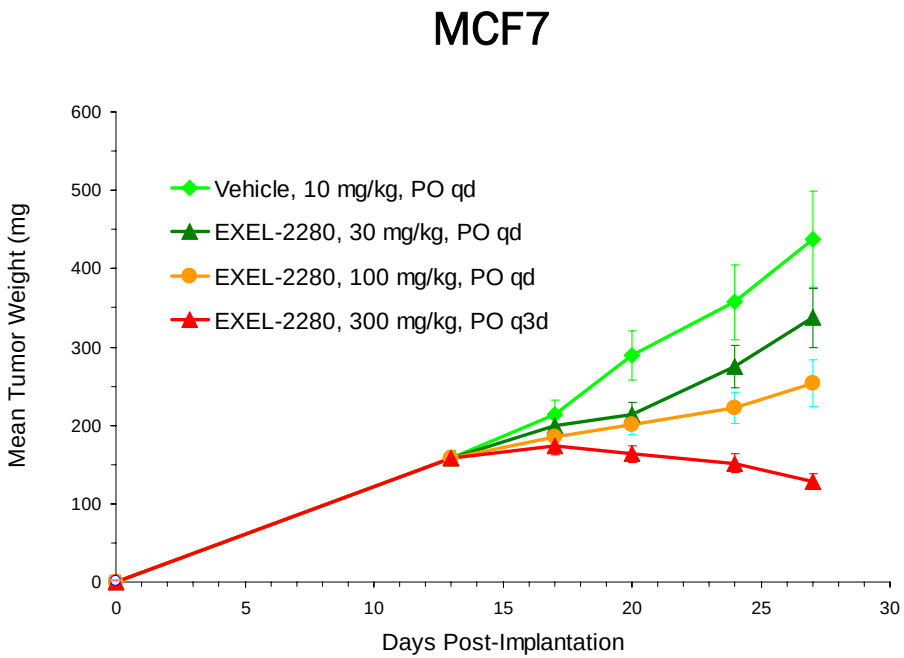
Significant in vivo PD effects on IGF1R and SRC pathways

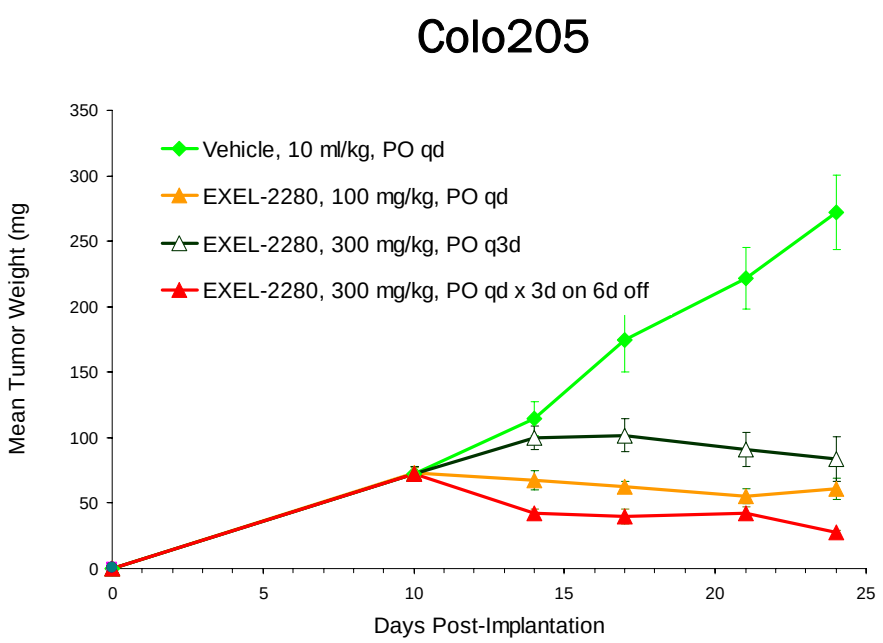
- Efficacious in multiple xenograft models



IND in 2006

XL228: In vivo Activity





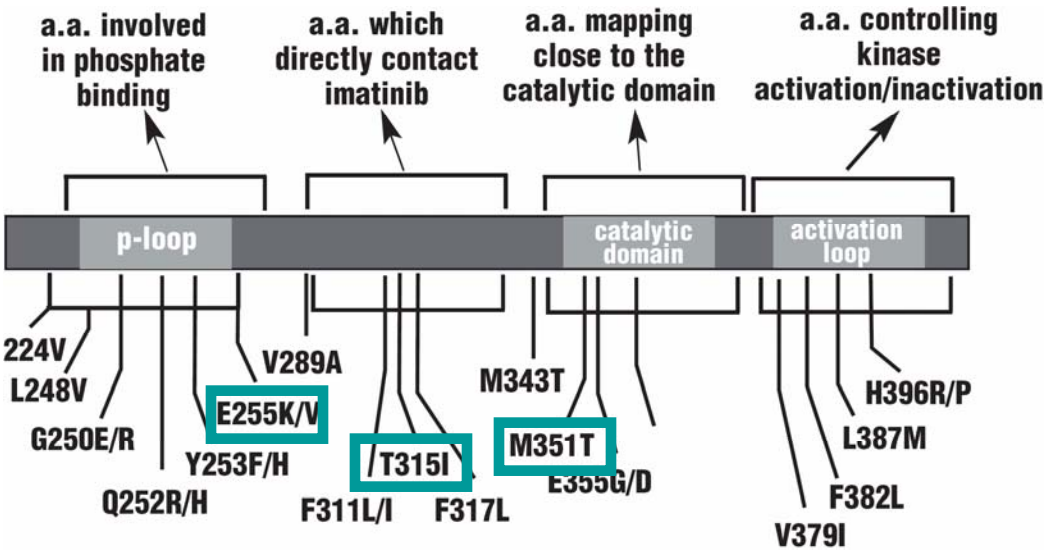
Tumor growth inhibition with regression at higher doses

XL228: Bcr-Abl Mutations

50-90% of patients with acquired resistance to Gleevec have mutations in the kinase domain of Bcr-Abl

E255K, T315I and M351T are the most frequent mutants

T315I mutation is highly resistant to 2nd generation Bcr-Abl/SRC inhibitors (e.g. dasatinib, AMN107)



Martinelli et al. Haematologica (2005)

Patients will relapse due to T315I mutations

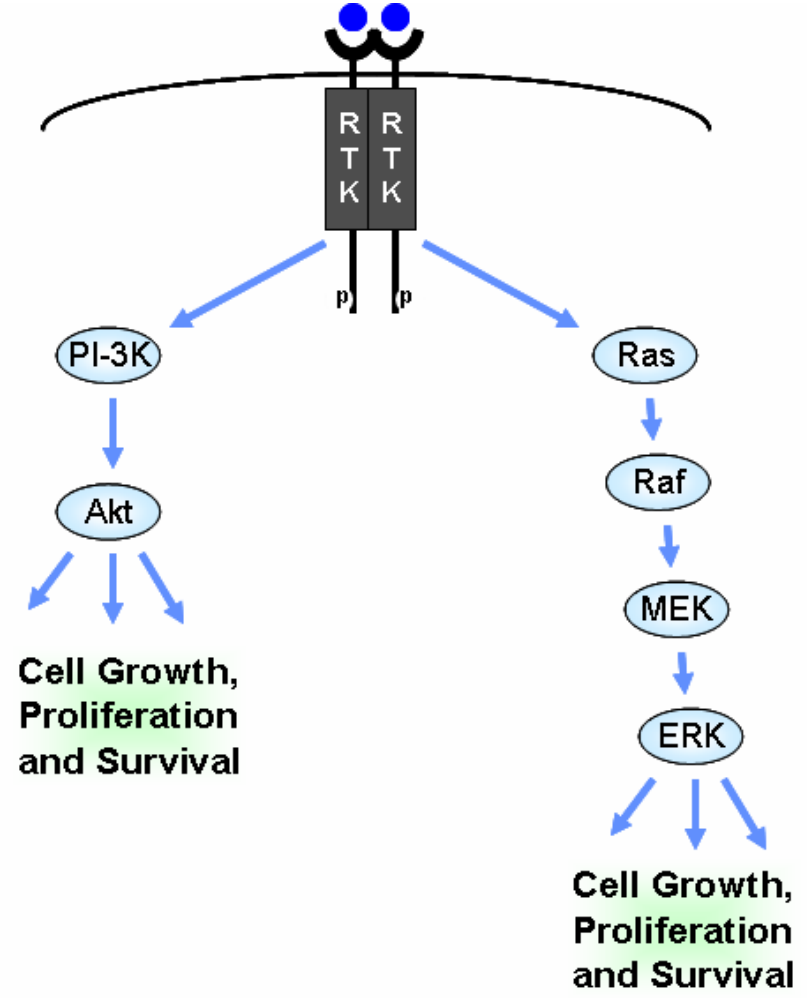
XL228 is a Potent Inhibitor of Mutant Abl

IC50 nM	WT Abl (active)	Abl T315I
XL228	8	4.5
imatinib	3270	>5000
dasatinib	0.6	>5000

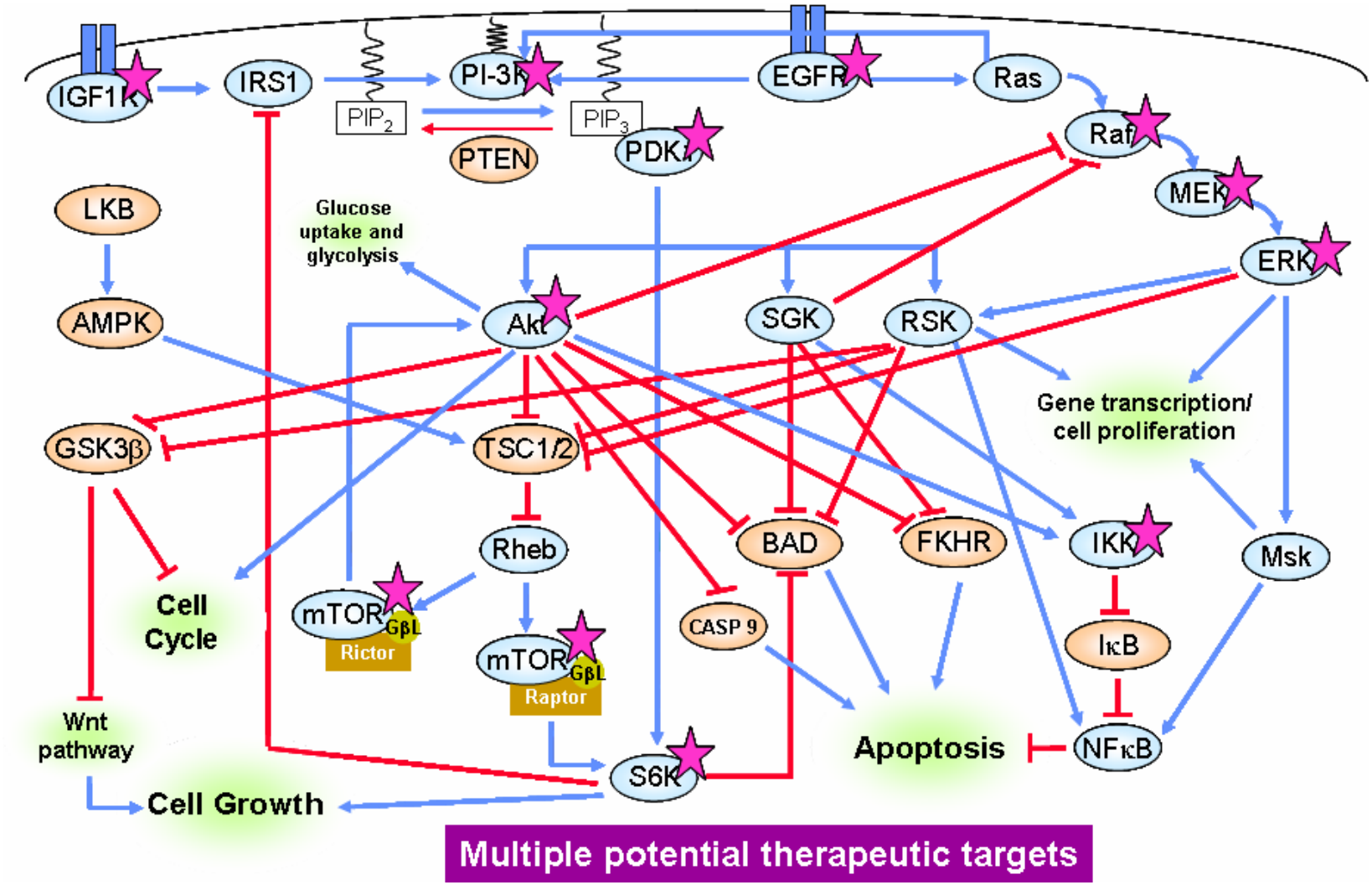
Active against Abl T315I mutant

Select imatinib and dasatinib resistant CML patients with T315I mutation for rapid clinical POC and registration

PI-3K/Ras Pathways



Second Generation Compounds: Signaling Downstream of RTKs



XL418: Low nM inhibitor of AKT and S6K

Targets multiple, critical nodes in growth, proliferation and survival pathways frequent upregulated in human tumors

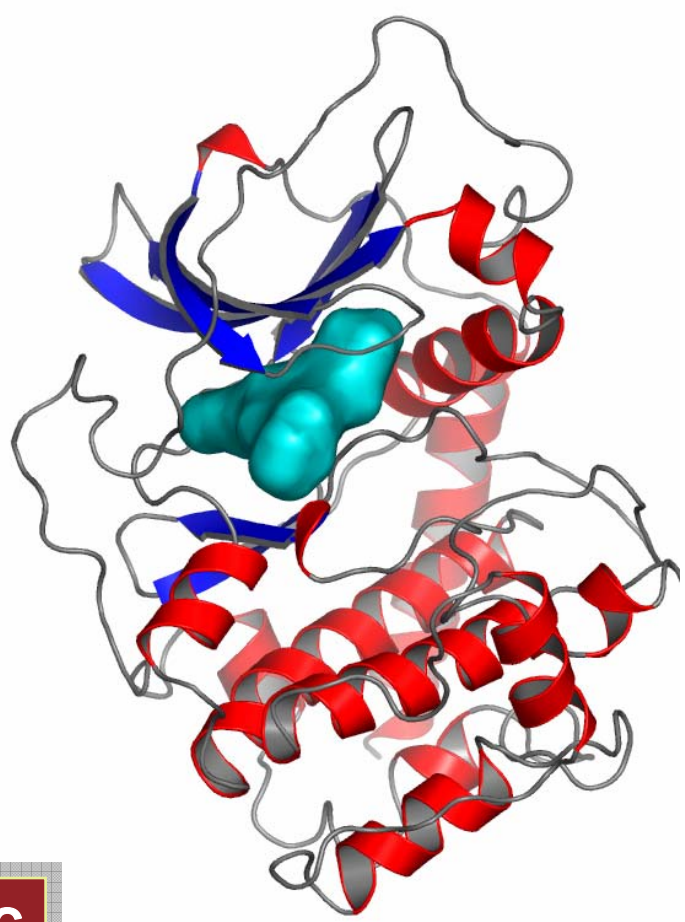
Inhibits tumor growth in vivo

- Favorable MOA distinction compared to rapamycin analogs

Potential for synergy with targeted and genotoxic therapies

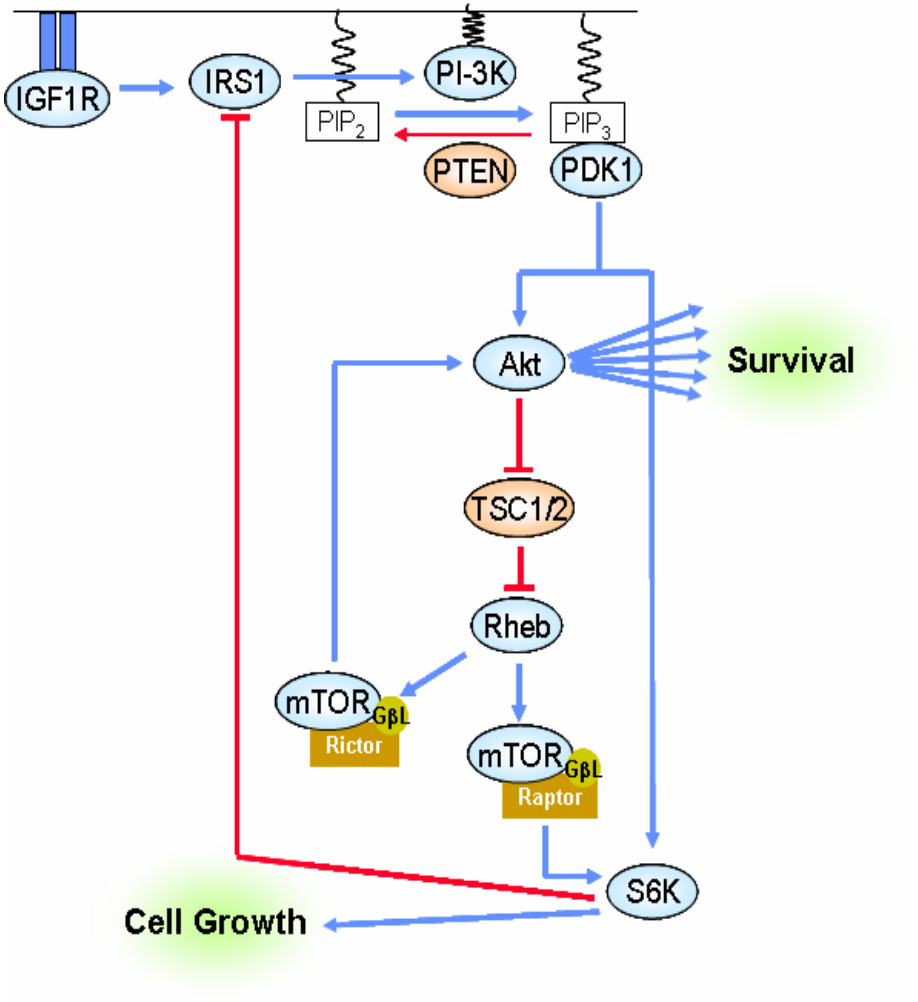
- Genotoxic/antimitotic agents, RTK inhibitors

Orally bioavailable, well tolerated



IND planned in 2006

PI3K/PTEN Pathway



AKT regulates multiple cell cycle/cell survival pathways

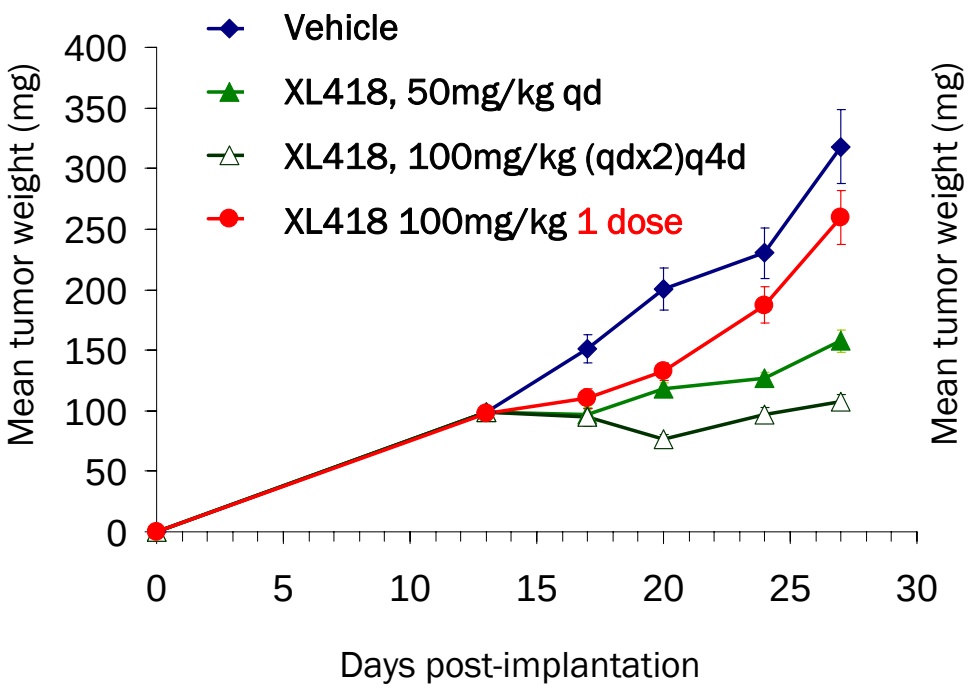
Negative feedback: Inhibiting mTOR/S6K upregulates AKT signaling

Rapamycin inhibits tumor proliferation but does NOT induce tumor apoptosis

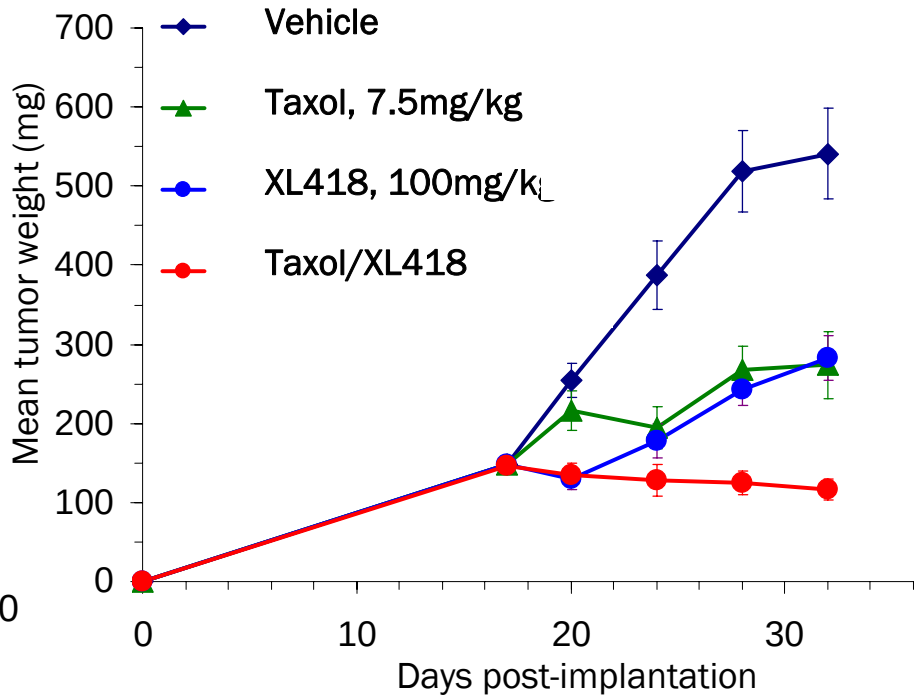
XL418 inhibits tumor proliferation AND induces tumor apoptosis

XL418: In vivo Activity

A549 lung adenocarcinoma



MCF7 breast carcinoma: enhancement of Taxol



XL281 - Summary

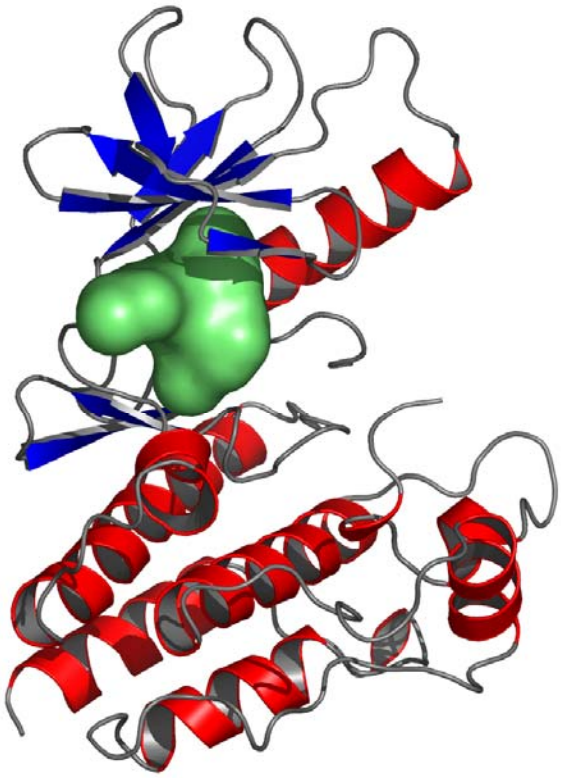
Highly potent & selective RAF inhibitor

- Optimized for potency: B-RAF, B-RAFV600E
- Inhibits the “active” B-RAF conformation
- Potent cell-based activity in mutant B-RAF and K-RAS cell lines

Good DMPK properties

Dual inhibition of p-MEK & p-ERK in vivo after oral dosing

Anti-tumor efficacy in five xenograft cell lines



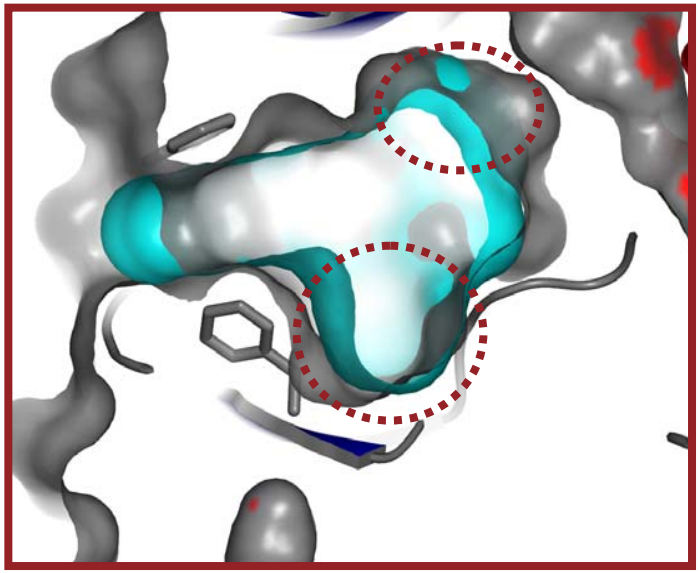
IND planned in 2006

XL281: In vitro Activity

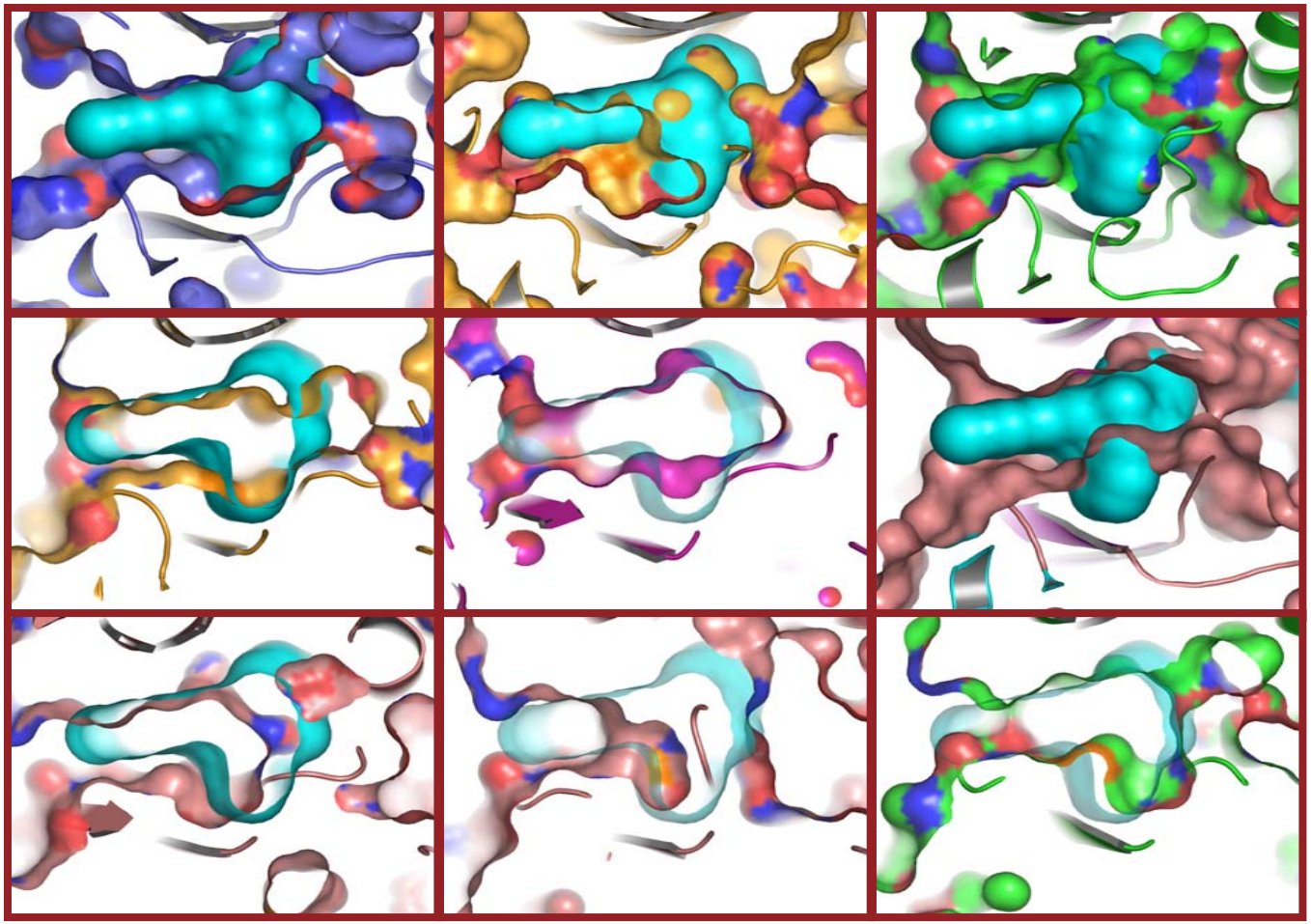
Kinase	IC_{50} (nM)
C-RAF	3.6
B-RAF	4.5
B-RAF V600E	5.0

Target	Cellular IC_{50} (nM)
MEK phosphorylation	22
ERK phosphorylation	28
Proliferation	1630

XL281 binds the active conformation of B-RAF

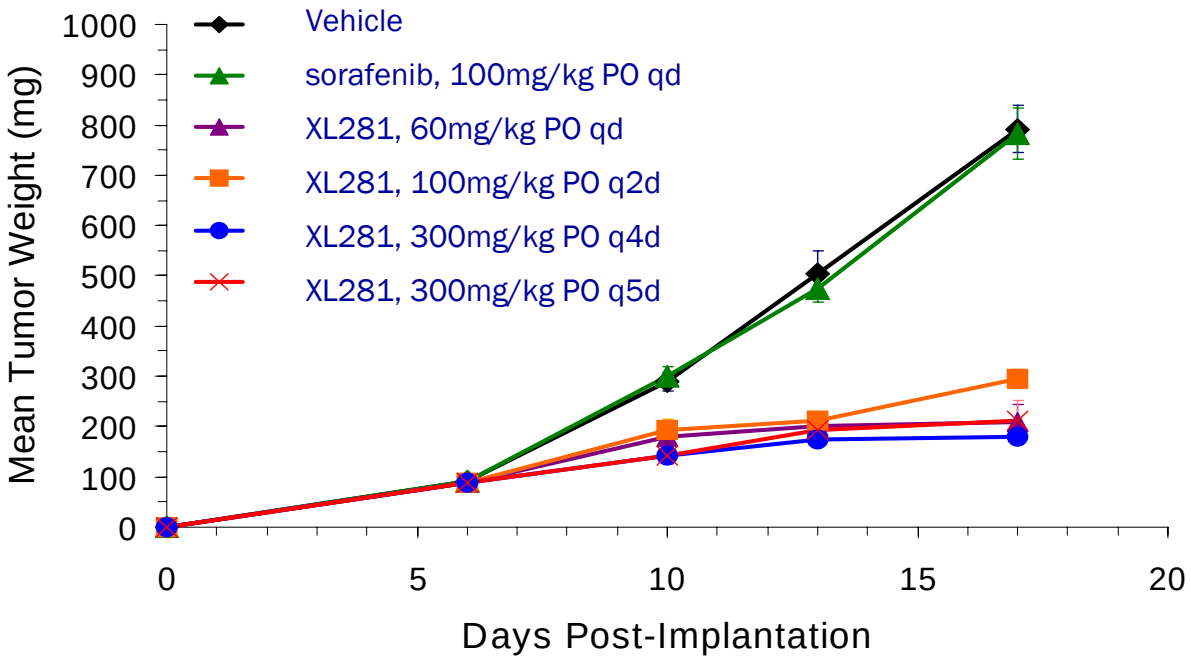


Exquisite Specificity of XL281



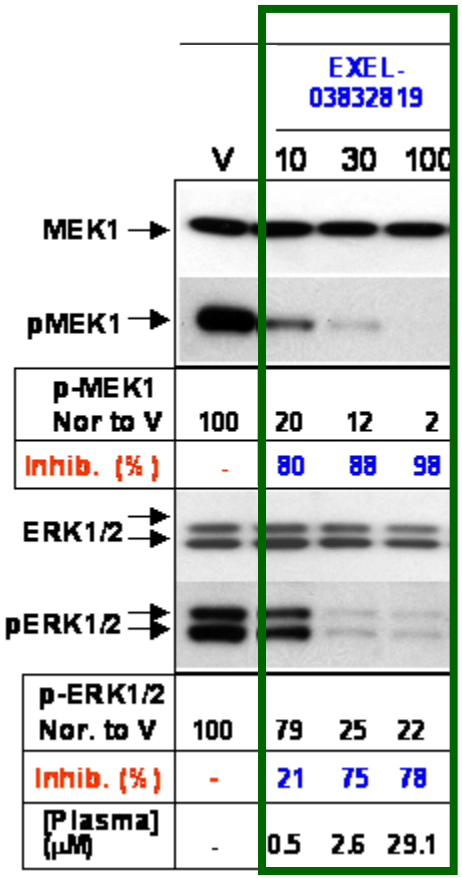
XL281 is not accommodated in the binding site of other kinases

XL281: In vivo Activity

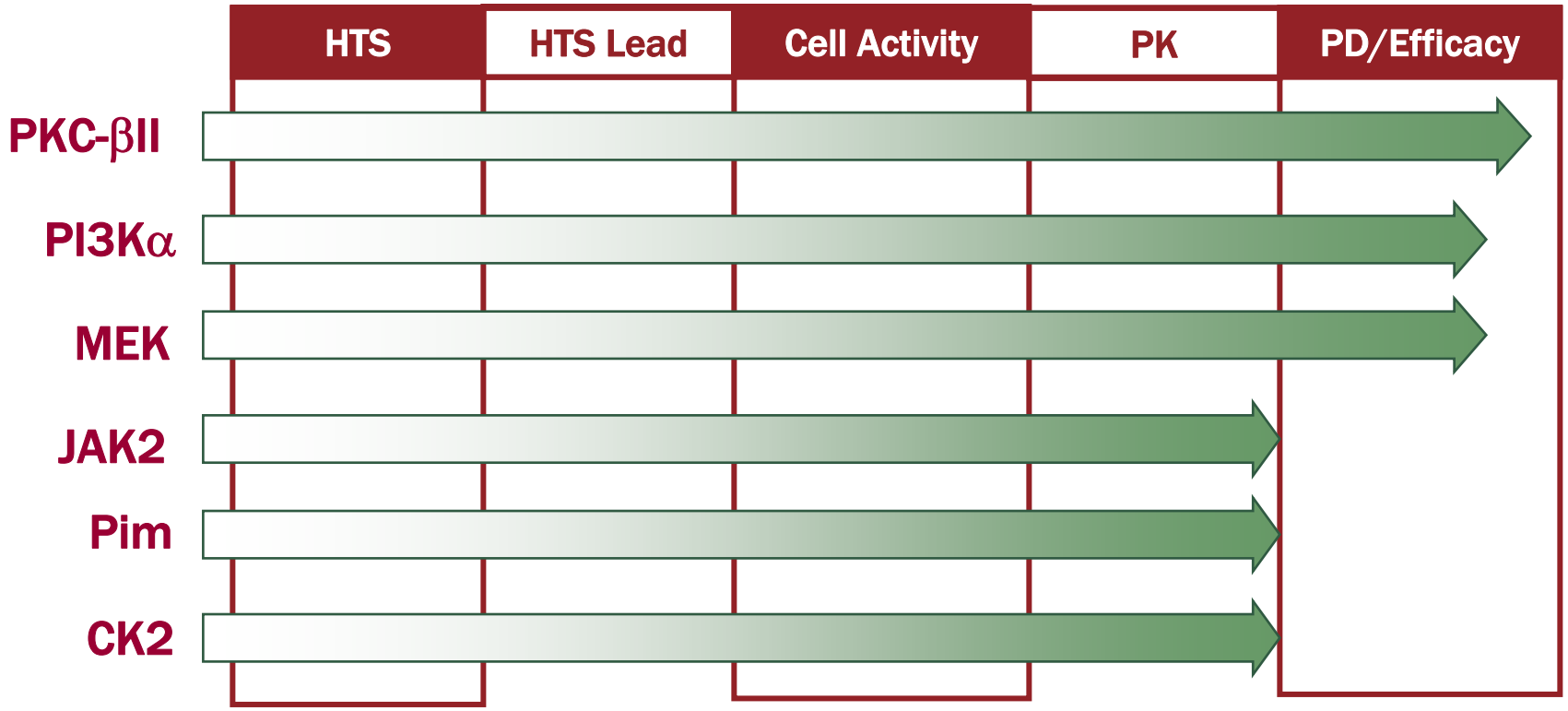


A431 xenograft model

In Vivo Target Modulation in MDA-MB-231 Model



Current Lead Op Projects – Potential 2006 DCs



Low nM leads with structural data driving final lead optimization

EXEL CV and Metabolic Disease Strategy

Acquire world-class NR targets and expertise

- X-Ceptor acquisition in 4Q 2004
- Strong NR biology platform and CV/metabolic disease expertise

Integrate NR biology into Exelixis discovery platform

- Full integration of NR targets and assays into Exelixis projects in 1Q05
- 3 CV/MD targets into full lead optimization (FXR, MR and LXR)
- 4Q05: FXR and MR advanced to DC & LXR at pre-DC stage

Broad focus on novel targets in NR and CV/MD space

- Additional NR targets in lead validation: GR, TR, AR, VDR

Partner compounds to advance assets clinically

- LXR partnered with BMS; FXR and MR assets in late stage discussions

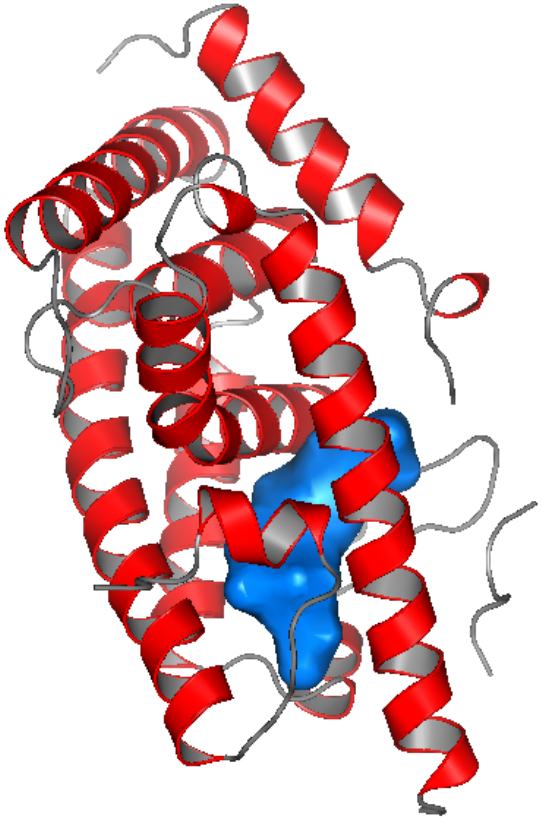
LXR and Atherosclerosis

Atherosclerosis

Primary mechanism of CAD and #1 leading cause of death in the USA

Need for therapy that attenuates disease pathology

- Macrophage inflammation
- Plaque stability and regression



LXR Agonists

Increase ABCA1 & reverse cholesterol transport

Inhibit inflammation at vessel wall

Display potent anti-atherogenic efficacy in established lesions

Challenge for an LXR Drug is to Maintain Anti-Atherogenic Effects in Macrophage and Minimize TG elevation in Liver

Summary of EXEL LXR Agonists

Multiple potent and novel scaffolds with unique molecular profiles

- Full agonists, partial agonists and dual LXR/FXR agonists

EXEL lead partial agonists display wide therapeutic window between ABCA1 induction & hepatic TG elevation in rodent models

- Potently induces reverse cholesterol transport
- Highly efficacious in atherosclerotic lesion prevention and regression
- Excellent overall safety in chronic efficacy models

Excellent DMPK and CYP profile

High oral bioavailability in mouse and monkey

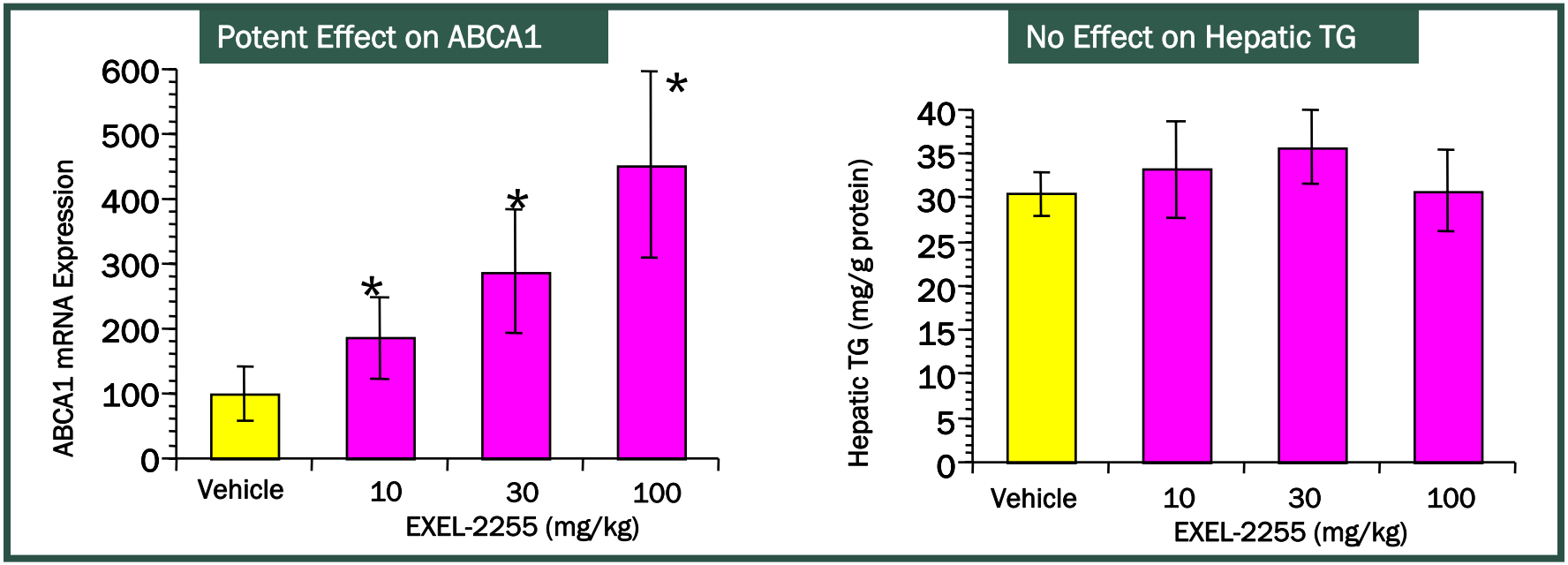
Identification of Pre-DCs in Dec 2005 and DC in 2006

LXR Agonist EXEL-2255: *In Vitro*, PK and PD Profile

LXRβ IC_{50} = 87 nM and ABCA1 EC_{50} = 440 nM

High selectivity in panel of 10 NRs > 100-fold

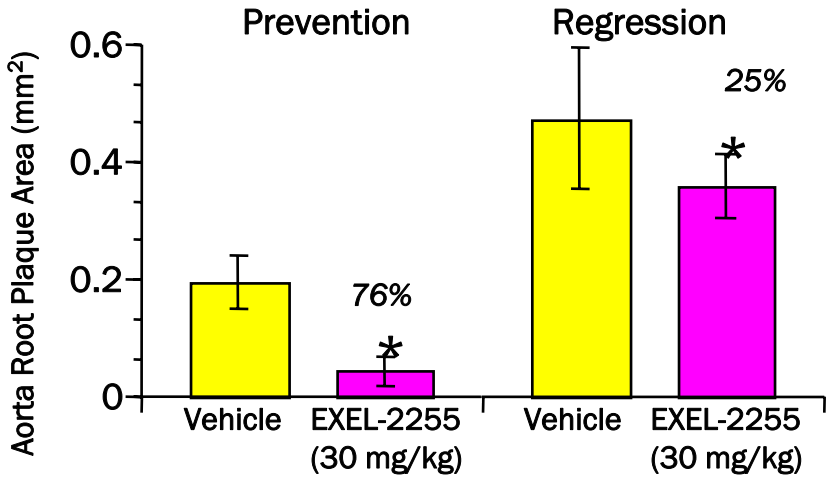
40-50% bioavailability in rats & cynos - no CYP/hERG liability



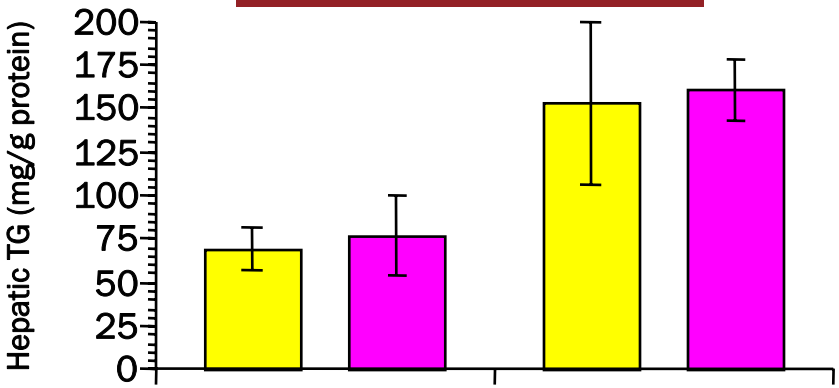
Potent & selective LXR modulator with good oral bioavailability
Excellent efficacy & safety in mouse PD model

LXR Agonist EXEL-2255 is Highly Efficacious in Mouse Atherosclerosis Prevention and Regression Models

Significant Reduction in Lesion Area

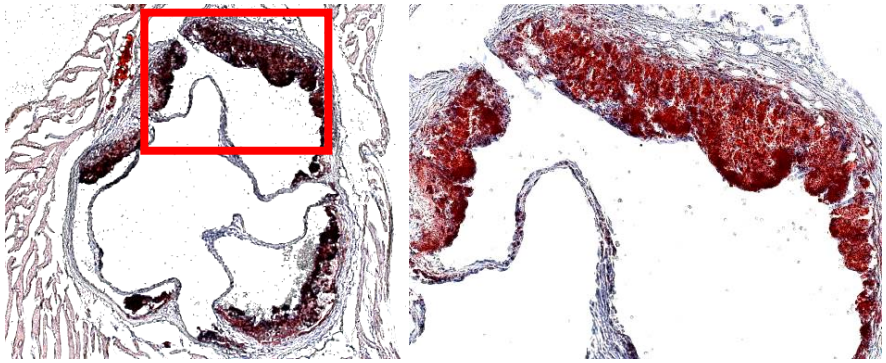


No Effect on Hepatic TG

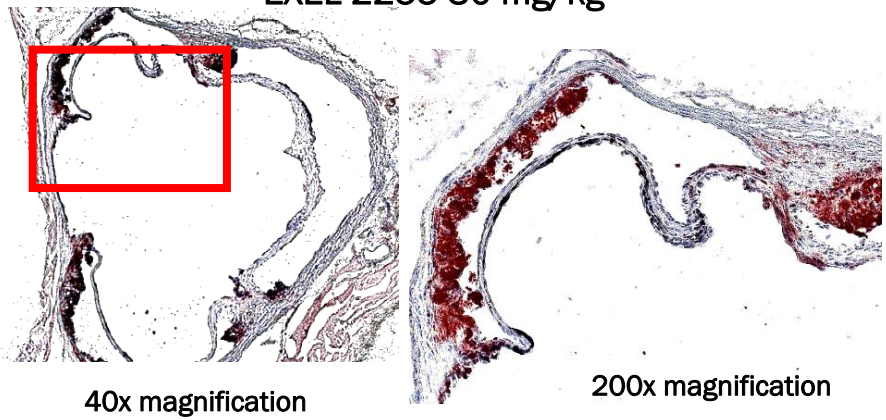


Prevention Study: Lipid (Oil Red O) Stain

Vehicle



EXEL-2255 30 mg/kg



40x magnification

200x magnification

XL335 - FXR Agonist Summary

Potent, selective, nonsteroidal FXR agonist

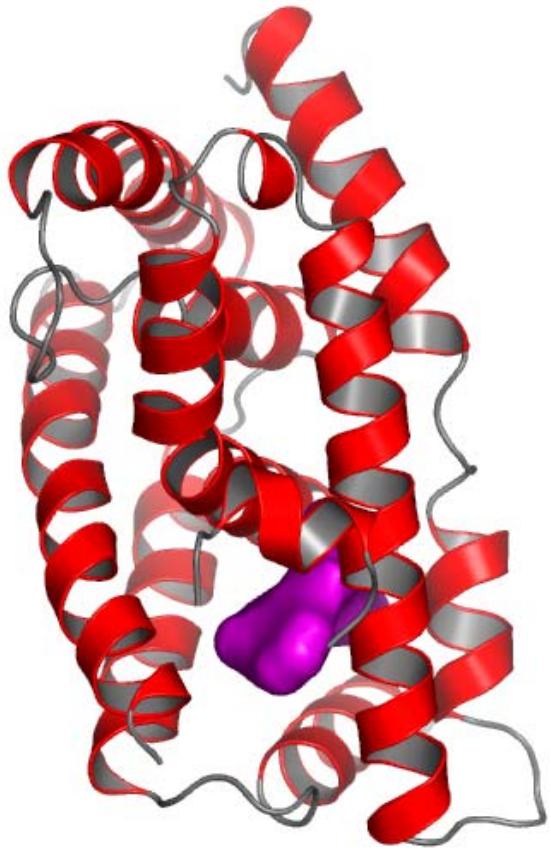
- Low cost of goods & excellent patent coverage

Efficacious at lipid reduction in multiple dyslipidemic models

- Regresses preexisting atherosclerosis
- Efficacious in models of fatty liver disease
- Efficacious in models of cholestasis and liver damage

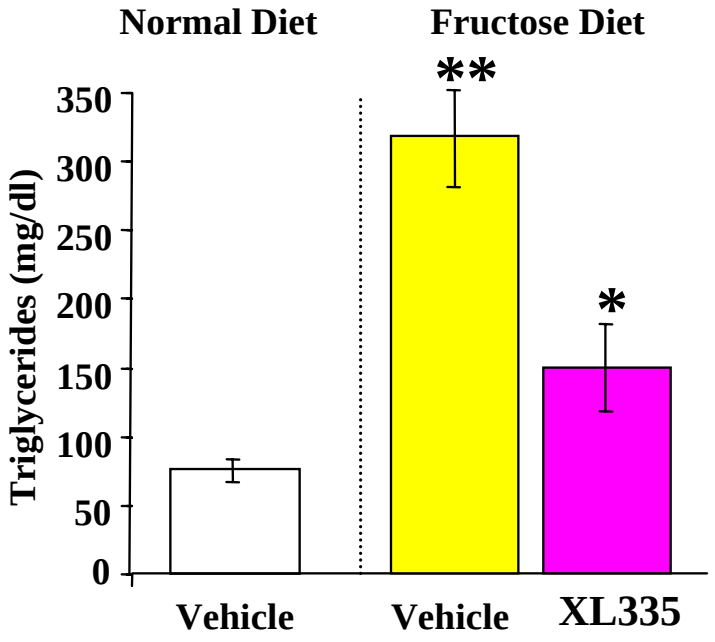
DMPK and Safety

- Excellent exposure and half life, no CYP liabilities
- No changes in clinical chemistry or hematology
- No histopathological changes

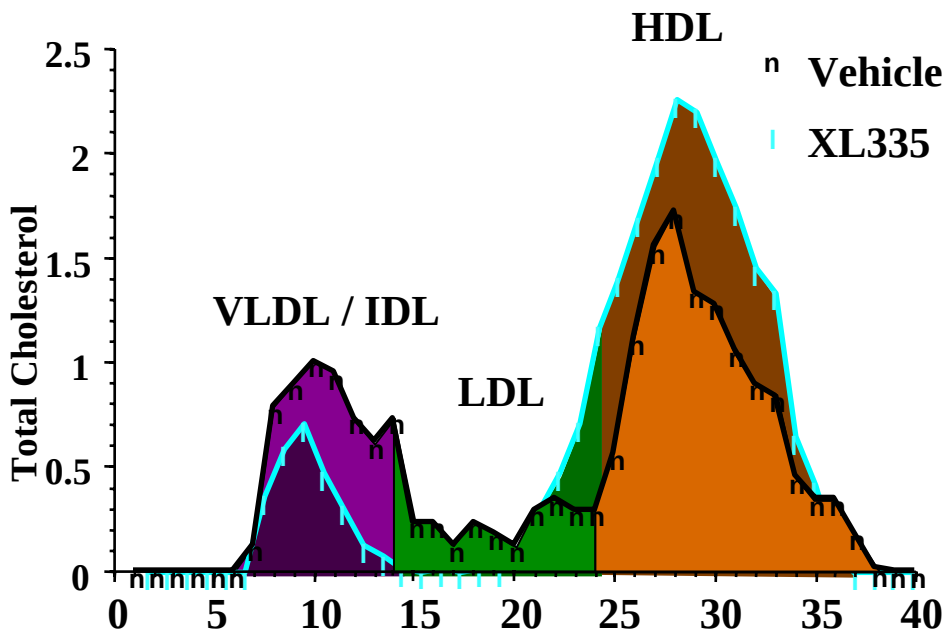


FXR Agonist XL335 Improves Plasma Lipid Profiles in Fructose-Fed Rats

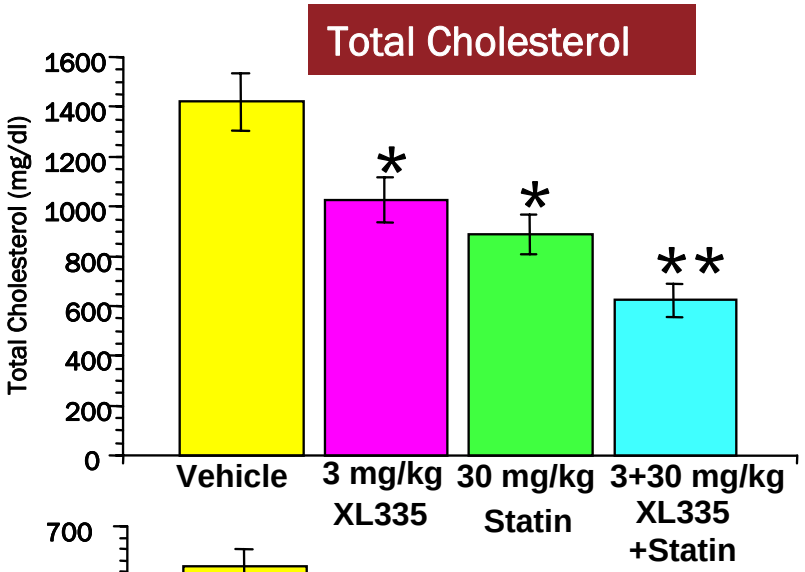
Plasma Triglycerides

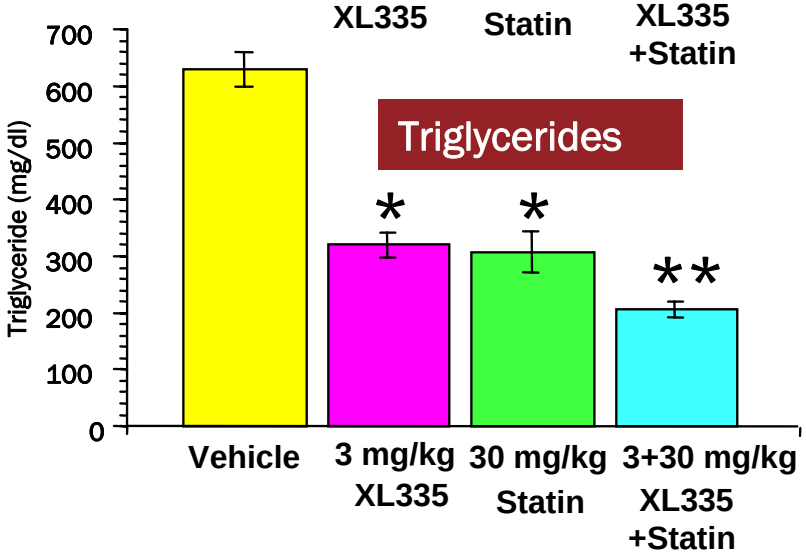


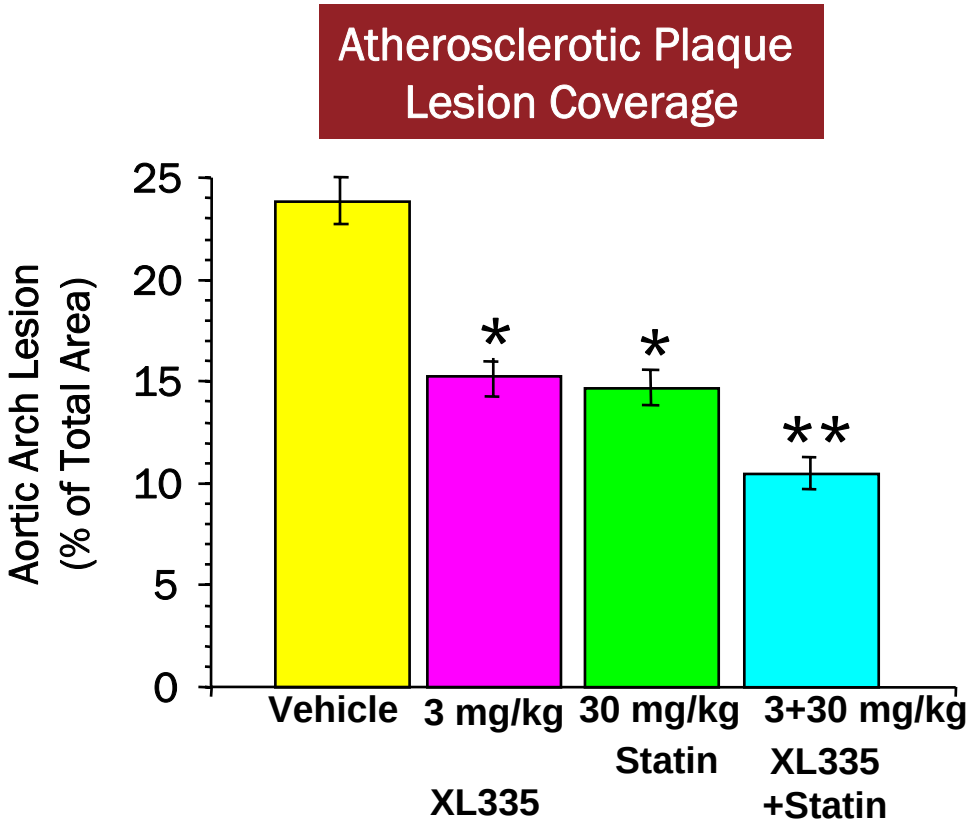
Plasma Cholesterol Profile



FXR Activation by XL335 Lowers Plasma Lipids, Decreases Atherosclerosis in LDLR-/- Mice



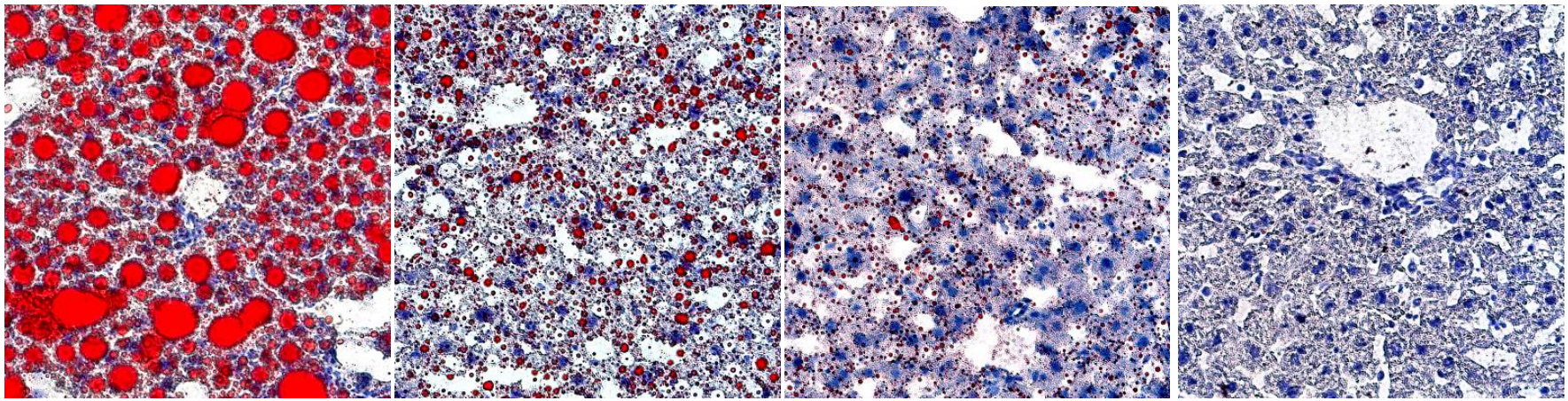




XL335 Reduces Fatty Liver Disease and Other Obesity-Related Symptoms in Diet-Induced Obese Mice

Western Diet Induced Obese Mice

Vehicle	XL335 30 mg/kg	XL335 100 mg/kg	Naïve Lean Mice



Reduces plasma lipids and reverses fatty liver disease

Marked improvement in markers of liver function

Decreases plasma fasting insulin - retains glucose clearance rates

XL550 - MR Antagonist Summary

Nonsteroidal MR antagonist

- More potent than Eplerenone
- More selective than Spironolactone
- Simple synthesis compared to steroids

Excellent DMPK properties

- High exposure and $t_{1/2}$ in multiple species
- No CYP liabilities = ideal for QD dosing

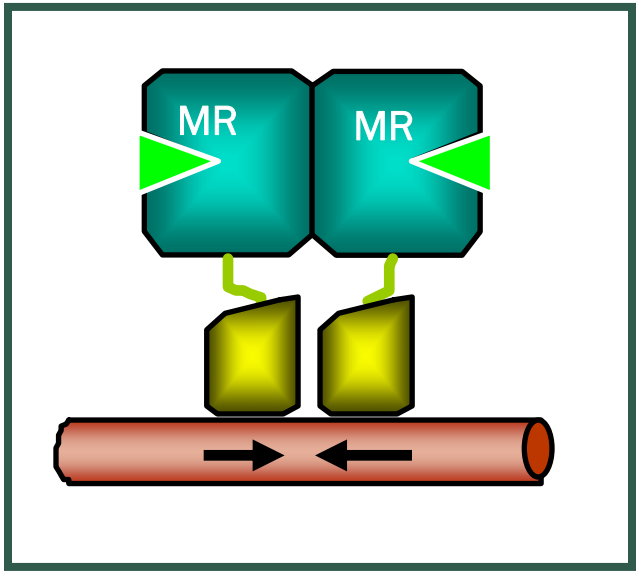
Potent & efficacious anti-hypertensive activity

- Completely blocks aldo-induced hypertension
- More efficacious than Eplerenone

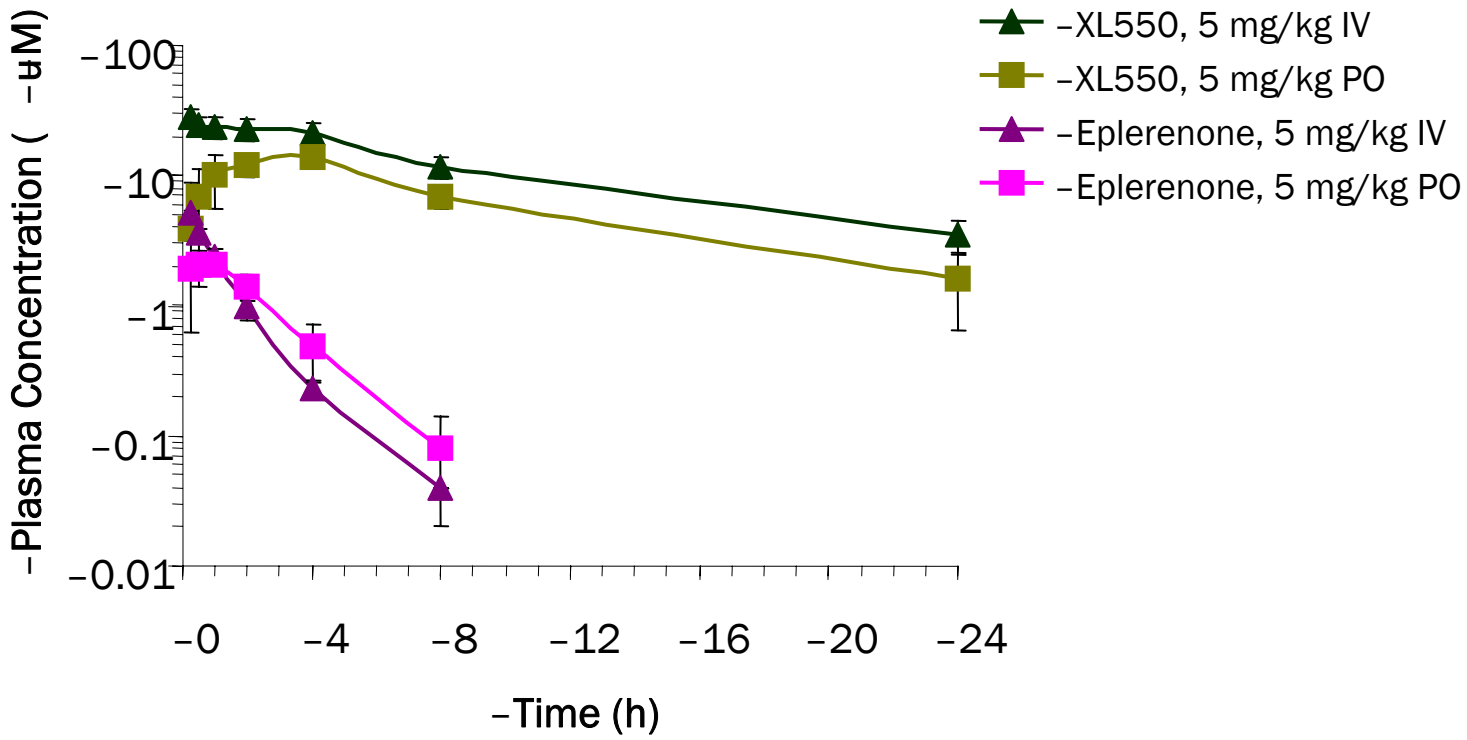
Protects against end-organ damage

- Cardio- and renal-protective
- Inhibits proinflammatory response

Outstanding safety profile



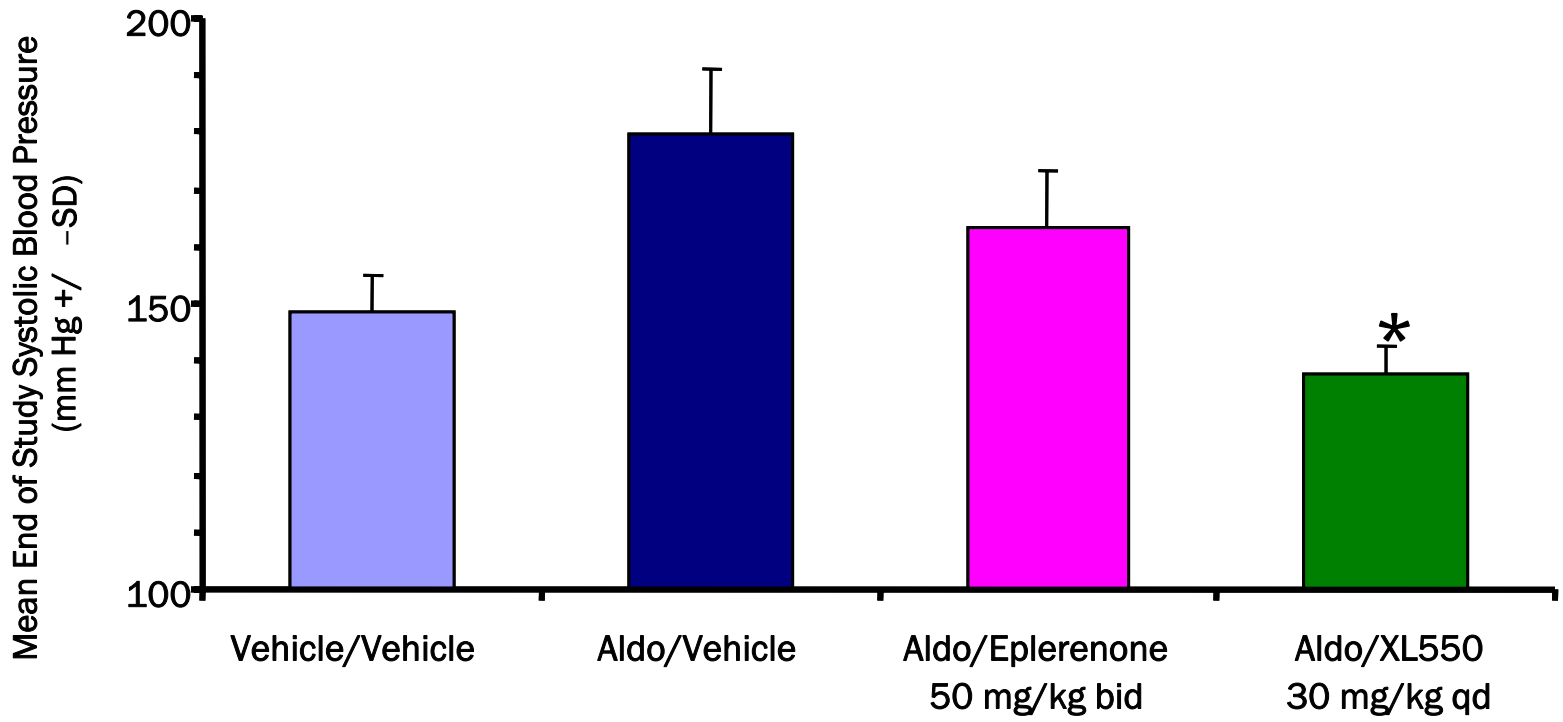
Rat PK Profile of XL550 and Eplerenone



	IV AUC/Dose	Bioavailability %F	PO Half-life (h)
Eplerenone	**1.5**	**86**	**1.4**
EXEL-8550	**53**	**51**	**7**

EXEL MR Antagonist has Excellent Anti-Hypertensive Efficacy Relative to Eplerenone

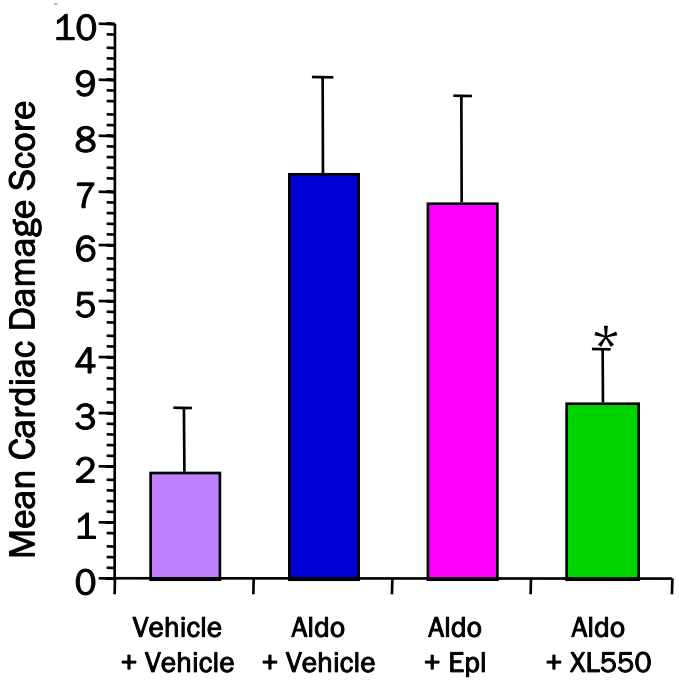
4-WK, Aldo-Infused, Salt-loaded, Uninephrectomized Rat Model

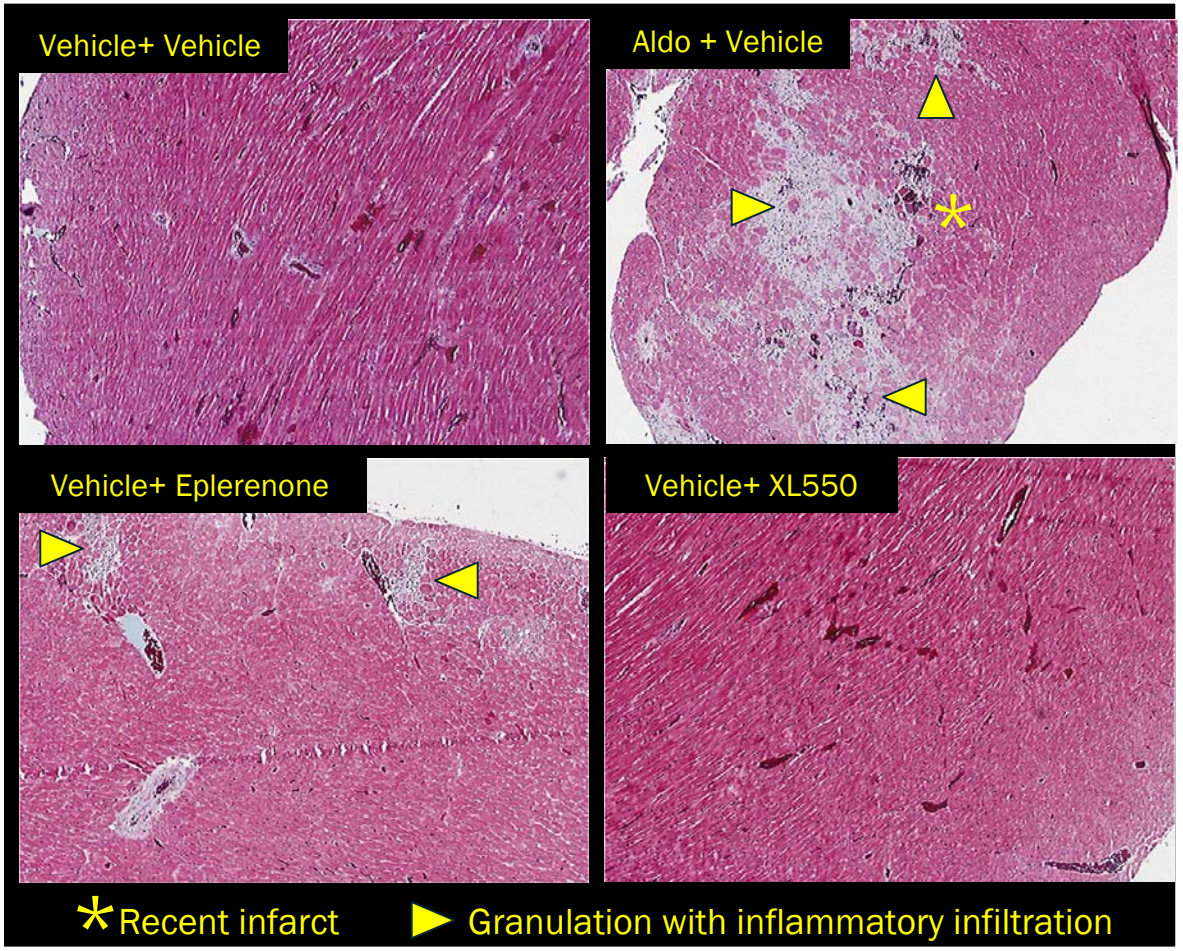


More efficacious (qd) than eplerenone (bid)

*p < 0.005 vs Aldo/Veh

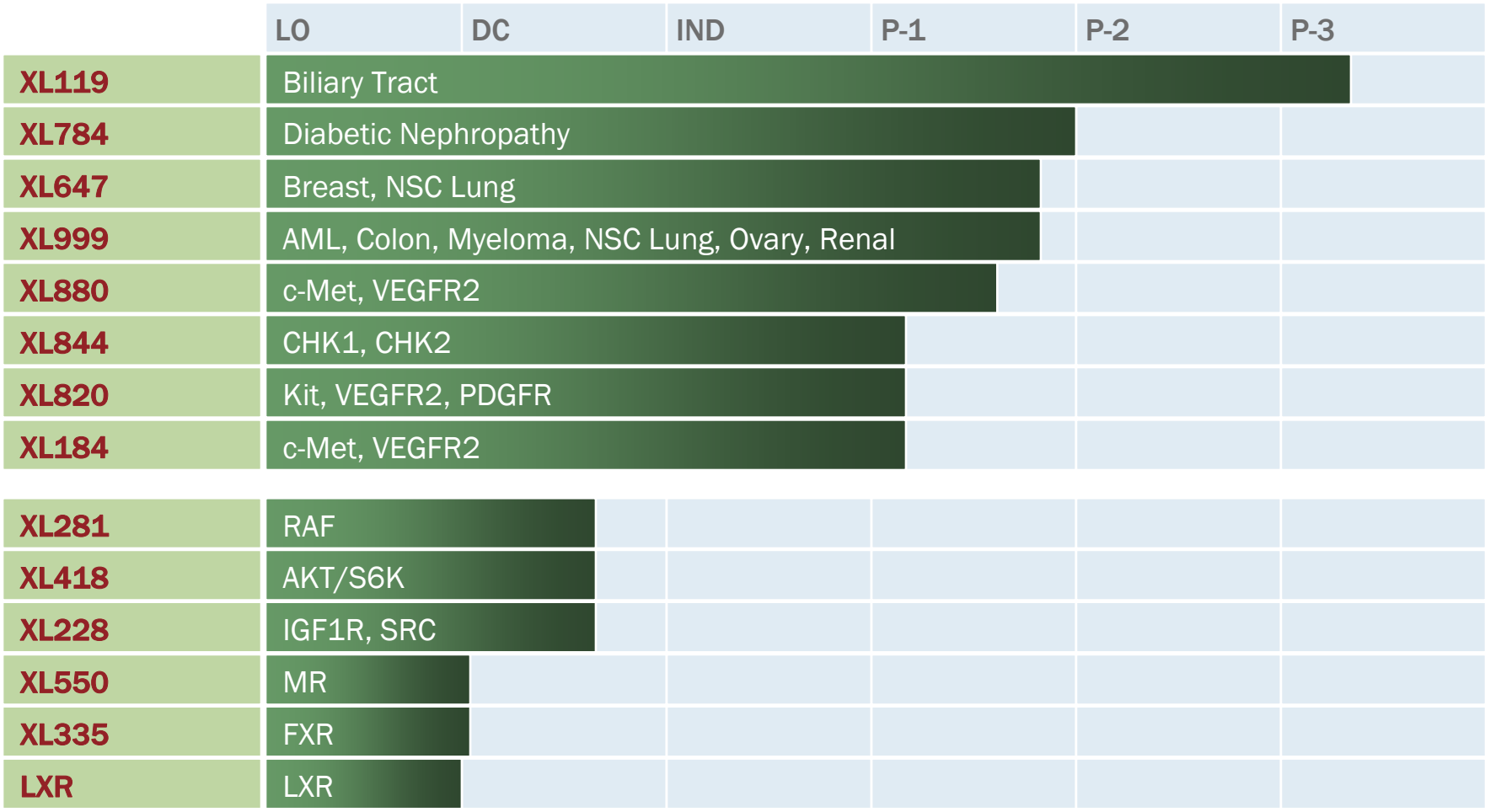
EXEL MR Antagonist, XL550 Has Excellent Cardiac Protection in Rat Model





Comparable renal protection seen in same animals

Exelixis Pipeline



Growing From a Solid Financial Foundation

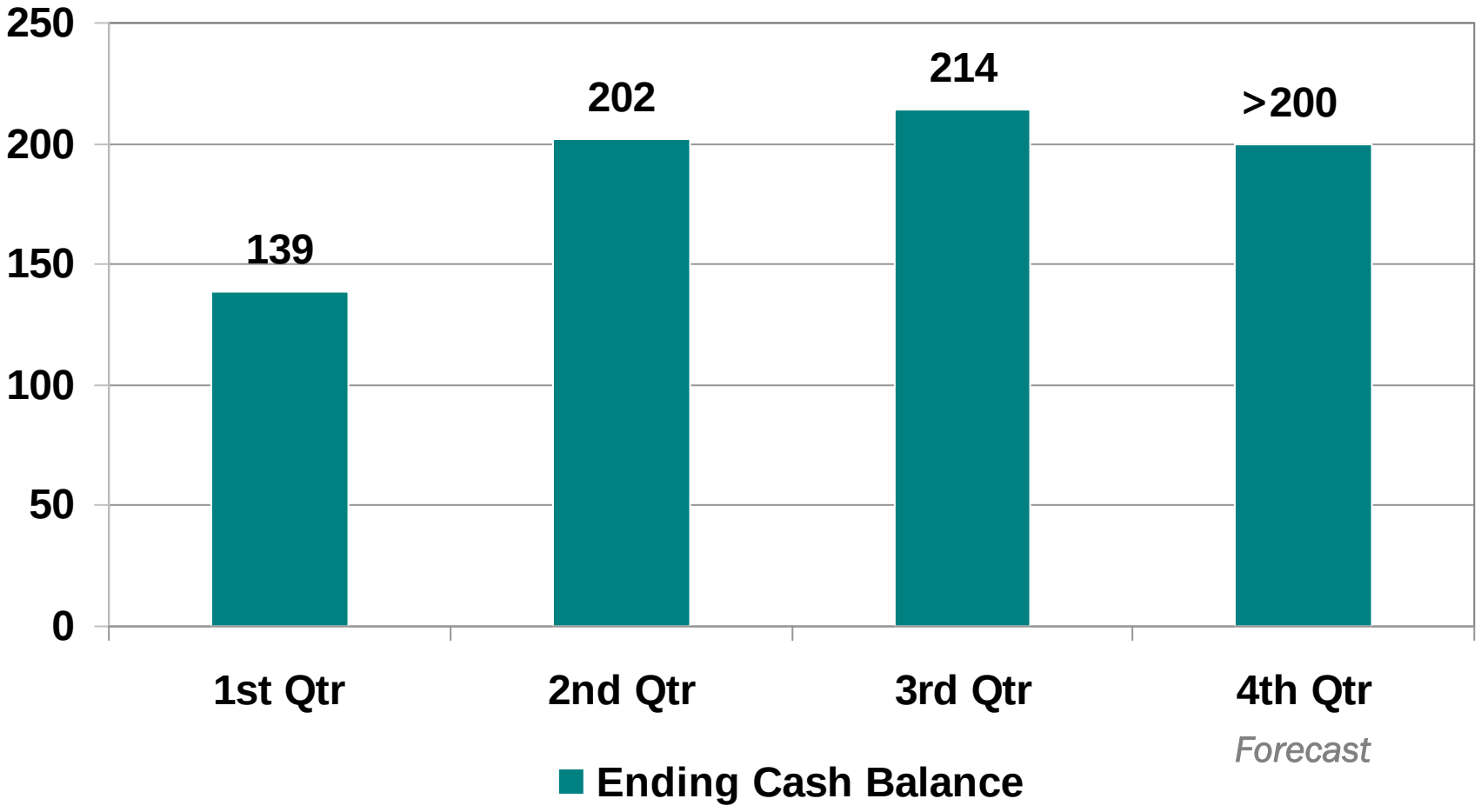
Financials* (in millions)

	2004A	2005E
Revenues	**$52.9**	**$75-80**
Operating Expenses**	**$158.5**	**$170-180**
Cash Balance	**$171.2**	**>$200**
Weighted Avg. Shares	**72.5**	**78.8**

* Additional information, including reconciliation of non-GAAP financial measures, is available in our quarterly financial press releases, available on our website at www.exelixis.com.

**Excluding restructuring expense, non-cash charges for stock compensation, acquired in-process research and development and amortization of intangibles.

2005 Cash Balance (in $ millions)



Financing Strategy:
Maximize Proceeds Minimize Dilution

FOUR PILLARS				
FUNDING SOURCES	**EXECUTE UNDER OUR EXISTING PARTNERSHIPS**	**PARTNER *SOME* OF OUR UNPARTNERED ASSETS**	**EXPLORE SUITABILITY OF FINANCING VEHICLES**	**ACCESS THE CAPITAL MARKETS**
OUTLOOK	• Significant R&D funding and milestones • GSK: Up to $240 million in product selection milestones • BMS (LXR): Approx. $140 million in development and regulatory milestones • Other: Genentech, BMS (Oncology)	• Partner Metabolism Programs • Partner compounds from GSK collaboration • New cancer collaboration(s)	• Additional clinical development financing vehicles	• Opportunistic financings
ACCOMPLISHED	• GSK milestones: $35 million • BMS milestones: $5.3 million	• Genentech deal: Up to $16 million • Helsinn deal: Up to $50 million • BMS (LXR) deal	• Symphony deal: Up to $80 million	• Equity Offering: $50 million

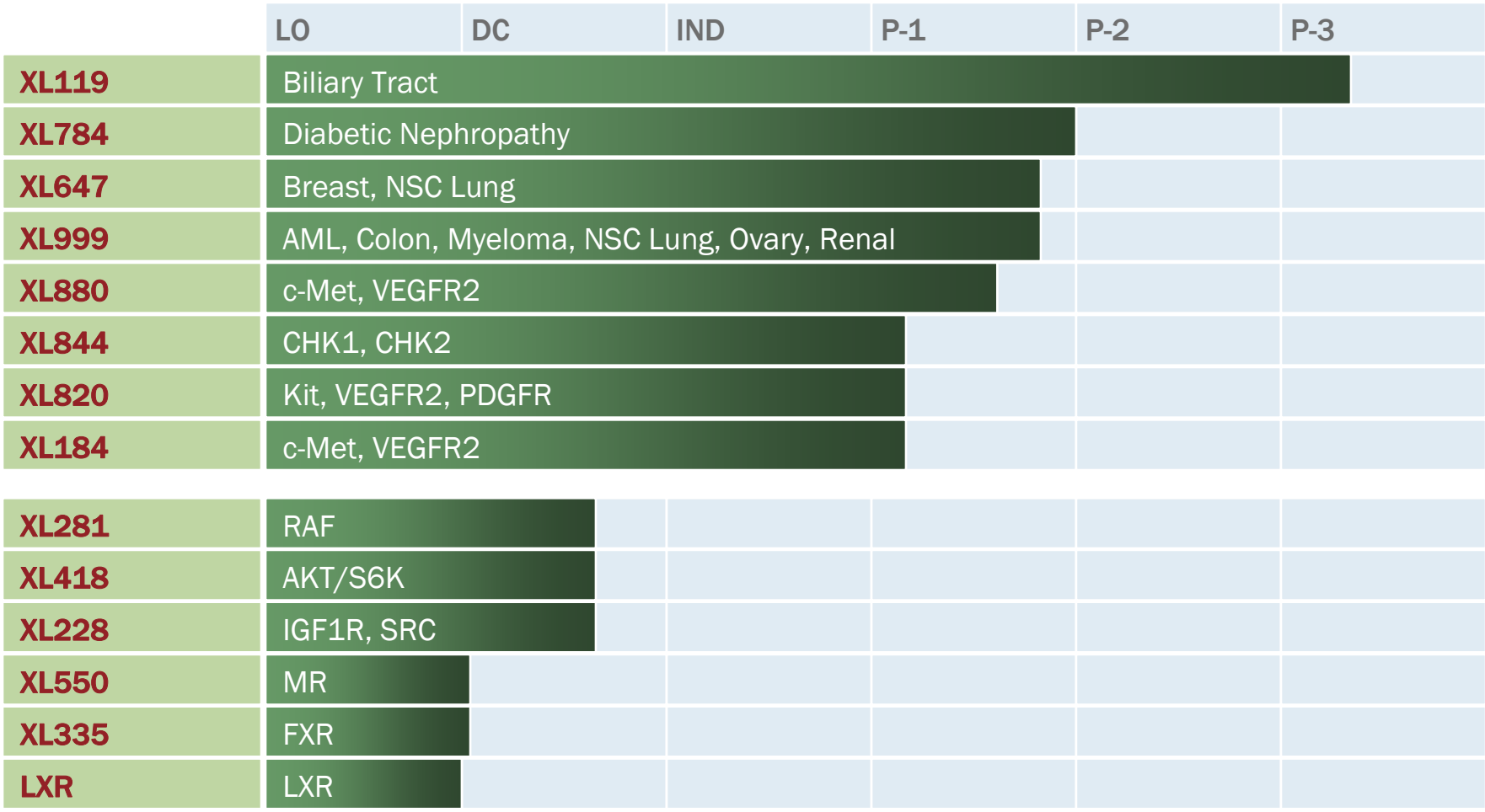
> $400 million in Potential New Funding from 2005 Deals

Charting Our Own Course
The First Annual Exelixis R&D Day

EXELIXIS™

December 6, 2005
Four Seasons Hotel, New York, NY

Exelixis Pipeline



Exelixis Pipeline

First-In-Class Compounds

- XL880: Dual c-Met/VEGFR inhibitor
- XL844: Selective Chk1/2 inhibitor
- XL281: Specific RAF inhibitor
- XL418: Dual AKT/S6K inhibitor

Best-In-Class Compounds

- XL647: EGFR/HER2/VEGFR
- XL999: VEGFR/FGFR/PDGFR
- XL184: Low pM VEGFR2 inhibitor
- XL784: MMP1 sparing ADAM10 & MMP2 inhibitor

Focus on Speed and Quality

Quality in Addition to Quantity

First 4 internally generated compounds demonstrated good pharmaceutical properties and are moving into Phase II

- No attrition from DC through Phase I trials
- Dosed at levels that resulted in good efficacy in animal models
- 3 orally administered (XL999 dosed IV)
- Good half-lives, Dose-proportional, Good DMPK

Half of pipeline directed to clinically validated targets

- Potential to be Best-In-Class
- Generally more potent in pre-clinical assays
- Unique spectrum of targets

Half of pipeline directed toward well-characterized targets

- Potential to be First-In-Class
- Highly potent, good DMPK properties in pre-clinical studies

Exelixis 2006 Goals and Upcoming Events

Phase II data

- XL999, XL647, XL880 (XL820?)

Rapid enrollment for XL784 Phase II trial

Phase I completion

- XL820, XL184, XL844

IND filings

- XL228, XL418, XL281

3-4 Proprietary development compounds

ASCO presentations (June)

EORTC presentations (November)

ASH presentations (December)

Additional collaborations and business transactions

Value Proposition

Large number of high-quality compounds

- Solid preclinical and CLINICAL data

Significantly enhanced upside potential

- More AND BETTER shots on goal
- Success of any one compound will drive company

Significantly reduced risk

- Failure of any one compound is not devastating

Solid financial position

Track record of execution and exceeding goals

Charting Our Own Course
The First Annual Exelixis R&D Day

EXELIXIS™

December 6, 2005
Four Seasons Hotel, New York, NY