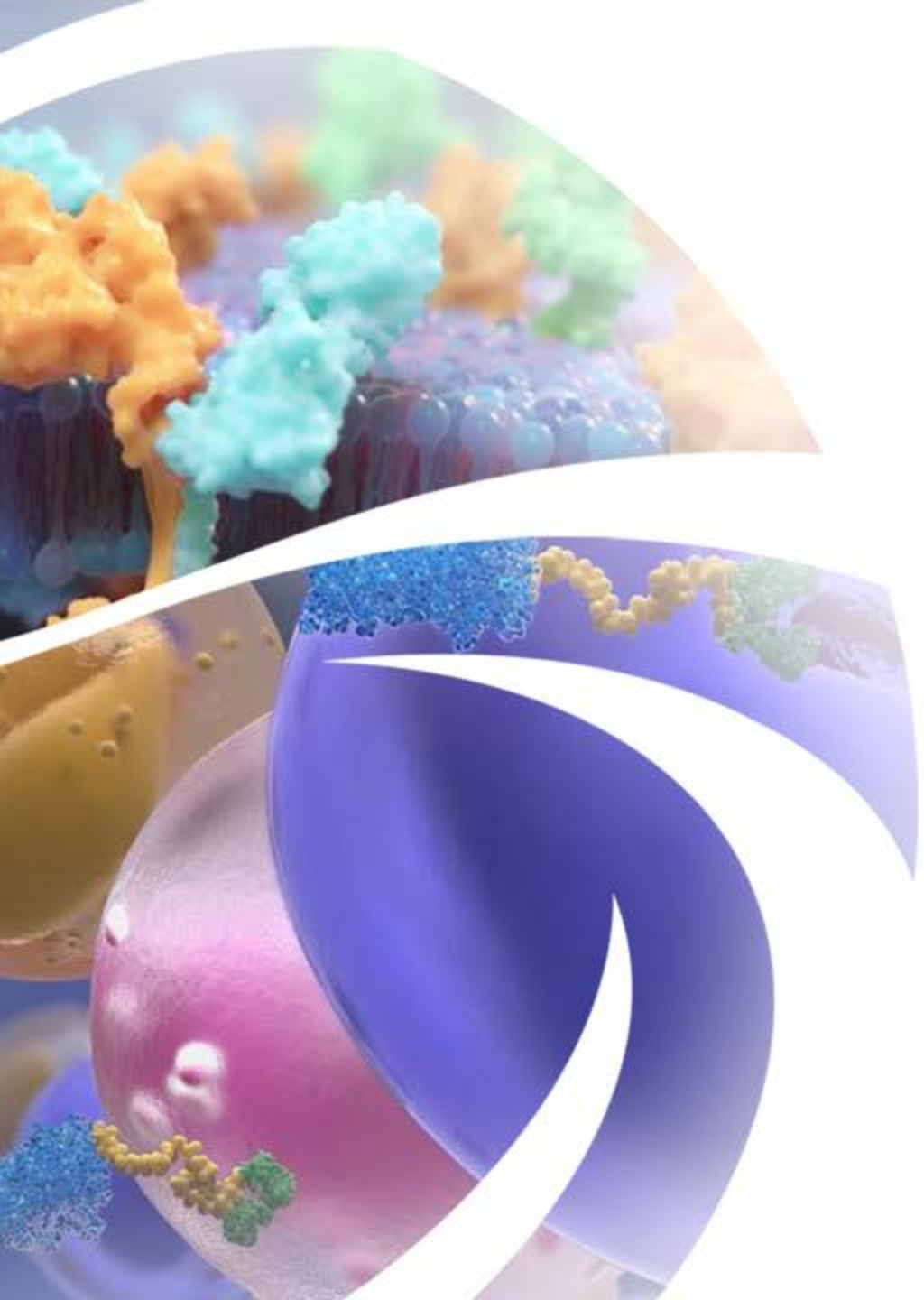

Welcome

Poziotinib:
Data Review and Program Strategy

April 28, 2020

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PHARMACEUTICALS
Redefining Cancer Care

Safe Harbor Statement

This presentation contains forward-looking statements regarding future events and the future performance of Spectrum Pharmaceuticals that involve risks and uncertainties that could cause actual results to differ materially. These statements are based on management's current beliefs and expectations. These statements include but are not limited to statements that relate to our business and its future, our strategy, the success of our drug candidates, the safety and efficacy of our drug products, product approvals, market potential, product sales, revenue, development, regulatory and approval timelines, product launches, product acquisitions, capital resources and any statements that relate to the intent, belief, plans or expectations of Spectrum or its management, or that are not a statement of historical fact.

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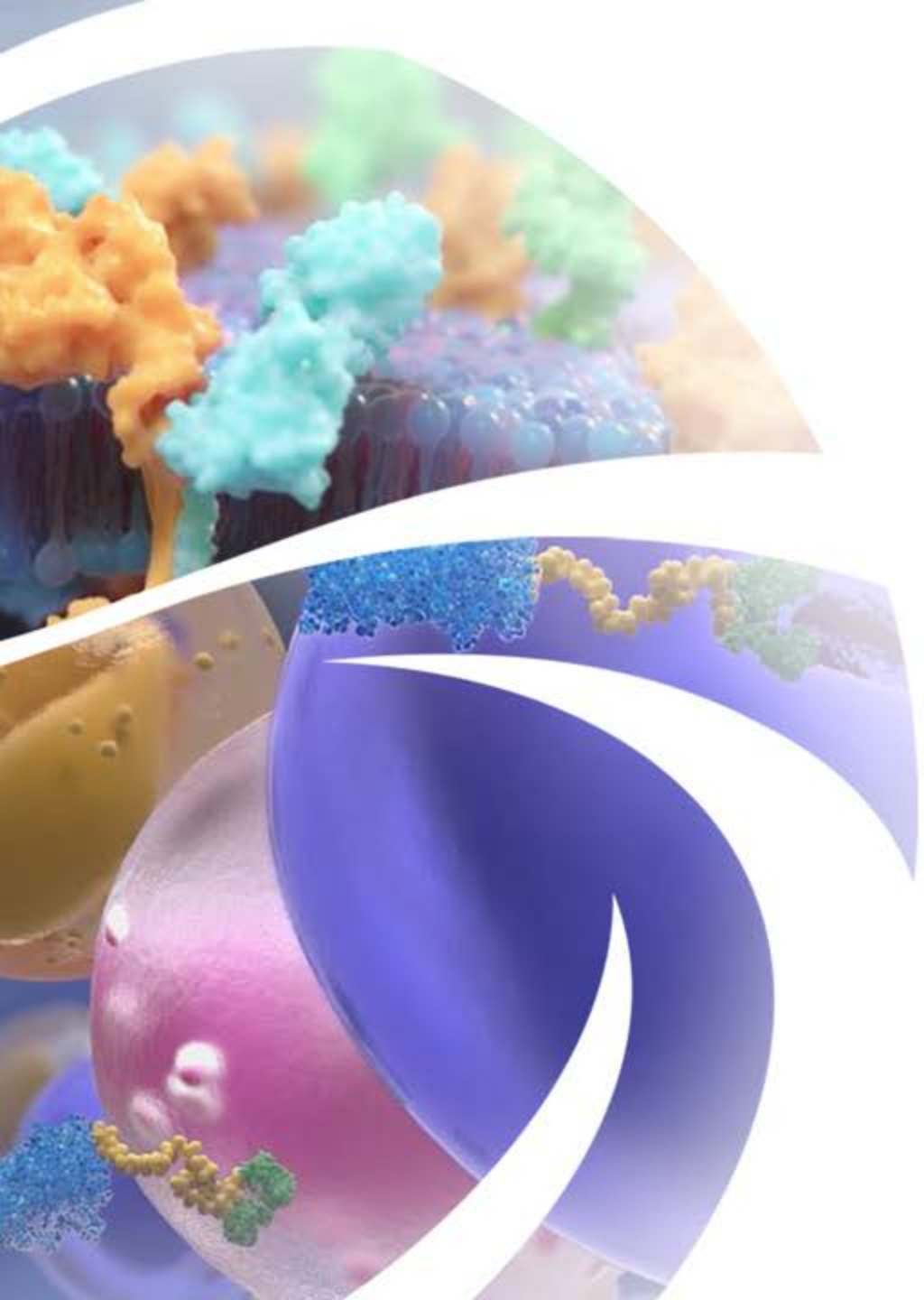

CEO Introduction

Joe Turgeon

April 28, 2020

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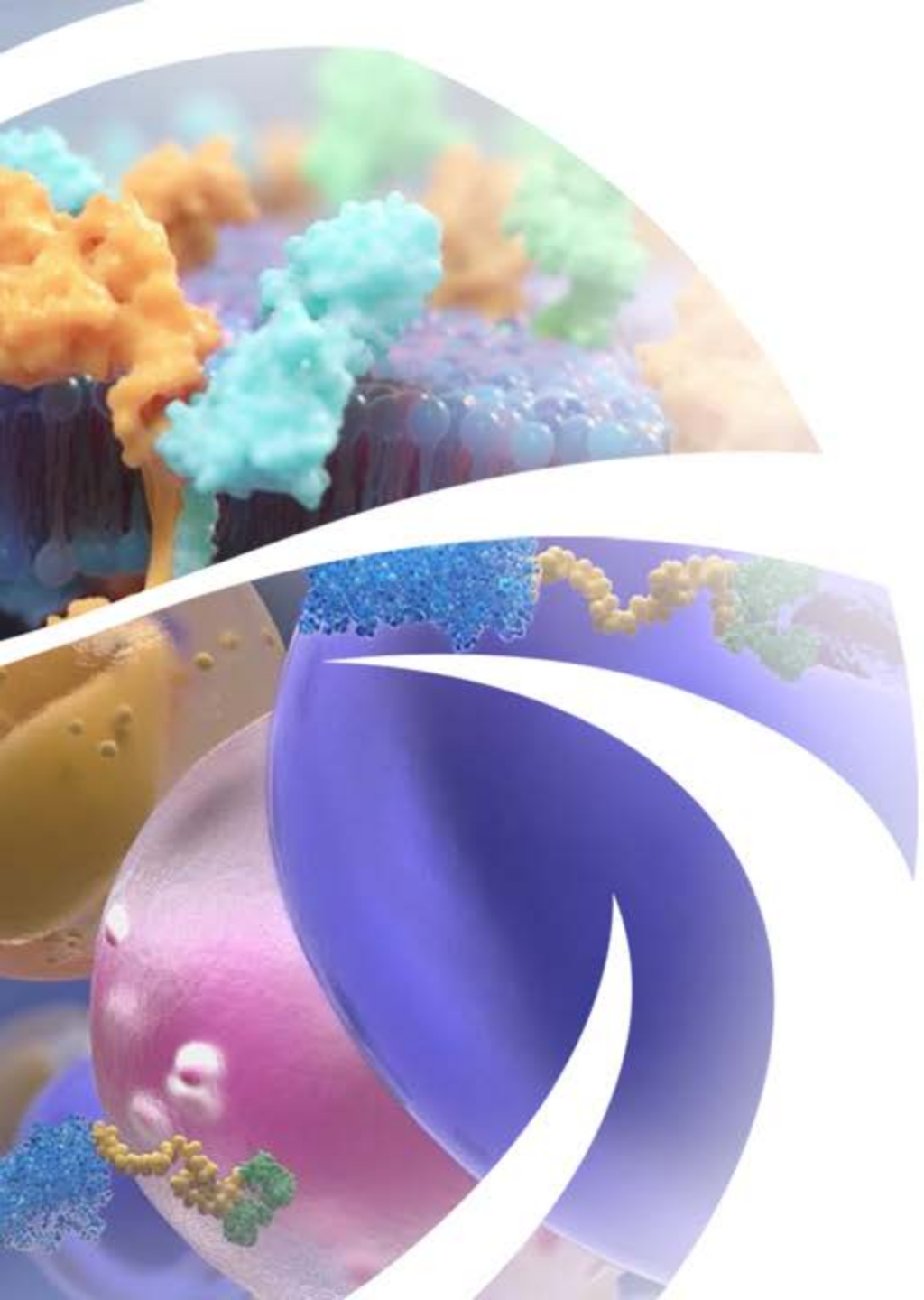

Phase 2 Study of Poziotinib in NSCLC with *EGFR exon20* Insertion

Mark A Socinski, MD

Chairman, Zenith20 Study Steering Committee

Former Co-Chair of the Thoracic Malignancies Steering Committee, NCI
AdventHealth, Orlando, Florida

April 28, 2020

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Disclosures

- **Honoraria**: Genentech, AstraZeneca, Merck, Guardant, BMS, Bayer
- **Consulting or Advisory Role**: Genentech, AstraZeneca, Merck, Guardant, BMS, Bayer
- **Speaker's Bureau**: Genentech, AstraZeneca, Bayer, Merck, Guardant, BMS
- **Research Funding**: Spectrum, Genentech, Novartis, AstraZeneca

Mark Socinski, MD PhD Chairman Steering Committee, ZENITH20 Study

Phase 2 study of poziotinib in NSCLC with *EGFR exon20* insertion

Xiuning Le[1]; Jonathan Goldman[2]; Jeffrey Clarke[3]; Nishan Tchekmedyian[4]; Zofia Piotrowska[5]; David Chu[6]; Gajanan Bhat[7]; Francois Lebel[7]; Mark A Socinski[8]

on behalf of ZENITH20 Study Group

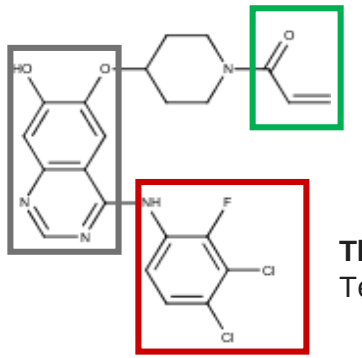
[1]MD Anderson Cancer Center, Houston, TX; [2]University of California, Los Angeles, Los Angeles, CA; [3]Duke University, Raleigh, NC; [4]Pacific Shore Medical Group, Long Beach, CA; [5]Massachusetts General Hospital, Boston, MA; [6]North Shore Hematology Oncology Associates P.C. [7]Spectrum Pharmaceuticals, Irvine, CA; [8]AdventHealth, Orlando, FL

Presented at 2020 AACR Plenary Session on Lung Cancer by Xiuning Le MD PhD, MDACC on 27 April 2020

Poziotinib is a Quinazoline-based EGFR Inhibitor

The small size and shape of poziotinib can fit to the binding pocket of exon20

Poziotinib

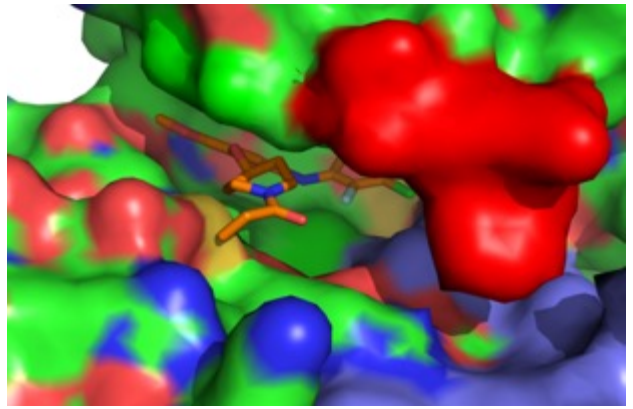


The body:
Quinazoline Core
(ATP mimetic)

The Arm:
Reactive Group (covalent bond to C797)

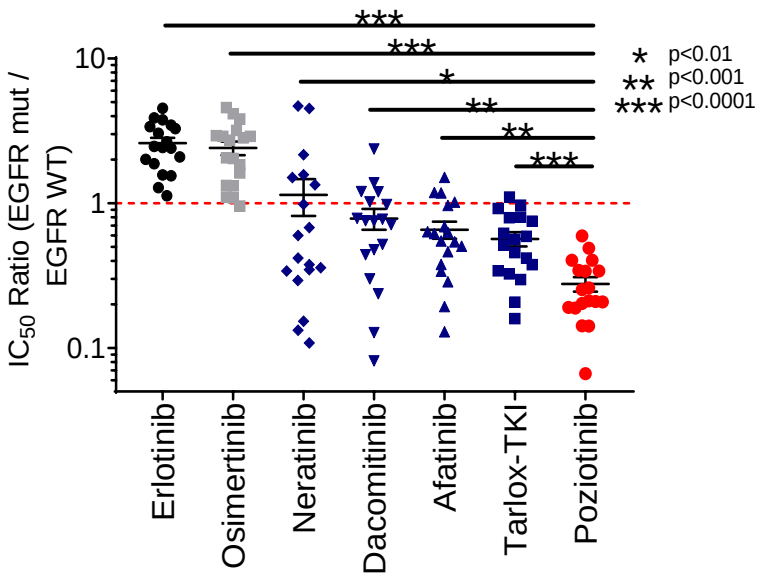
The feet:
Terminal group

EGFR D770insNPG

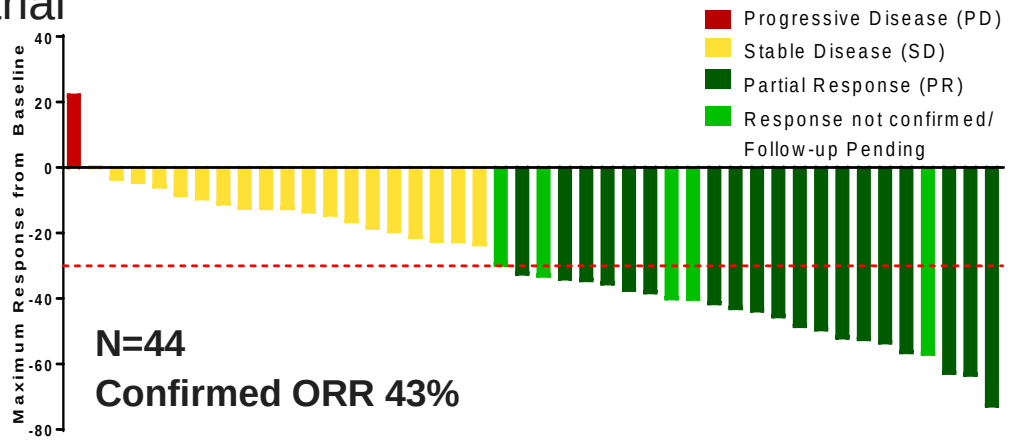


In vitro efficacy

EGFR Ba/F3 Selectivity Index
(N=20 cell lines)



Clinical efficacy in a single-center phase 2 trial



Robichaux, Heymach et al. Nat Med 2018, Heymach WCLC 2018

Virtual Annual Meeting Plenary Clinical Trial Abstract: 10189

Presenter: Xiuning Le

ZENITH20: A Pivotal Multi-center Phase 2 Study in North America and Europe

NSCLC patients with EGFR or HER2 exon 20 insertions

Key Eligibility Criteria

- NSCLC EGFR or HER2 exon20 insertions
- Point mutations, including T790M, are not allowed
- Brain mets are allowed if stable

Cohort 1
EGFR - previously treated
(N = 87)

Cohort 2
HER2 - previously treated
(N = up to 87)

Cohort 3
EGFR - treatment naive
(N = up to 70)

Cohort 4
HER2 - treatment naive
(N = up to 70)

Oral daily dose
28-day cycle

Poziotinib
16mg QD

Primary Endpoint

- Objective Response Rate (RECIST 1.1 by IRC)

Secondary Endpoints

- Disease Control Rate (DCR)
- Duration of Response (DoR)
- PFS (exploratory)
- Safety

Baseline Patient and Tumor Characteristics (N=115)

Characteristic		N (%)
Median age, years (range)		61 (33, 83)
Sex	Female	77 (67)
Race	White	77 (67)
	Asian	18 (16)
Smoking history	Never smoker	79 (69)
	Former smoker	2 (2)
	Regular smoker	34 (30)
Prior lines of therapy	1	49 (43)
	2	29 (25)
	≥3	37 (32)
Prior EGFR TKI therapy	Yes	29 (25)
	No	86 (75)

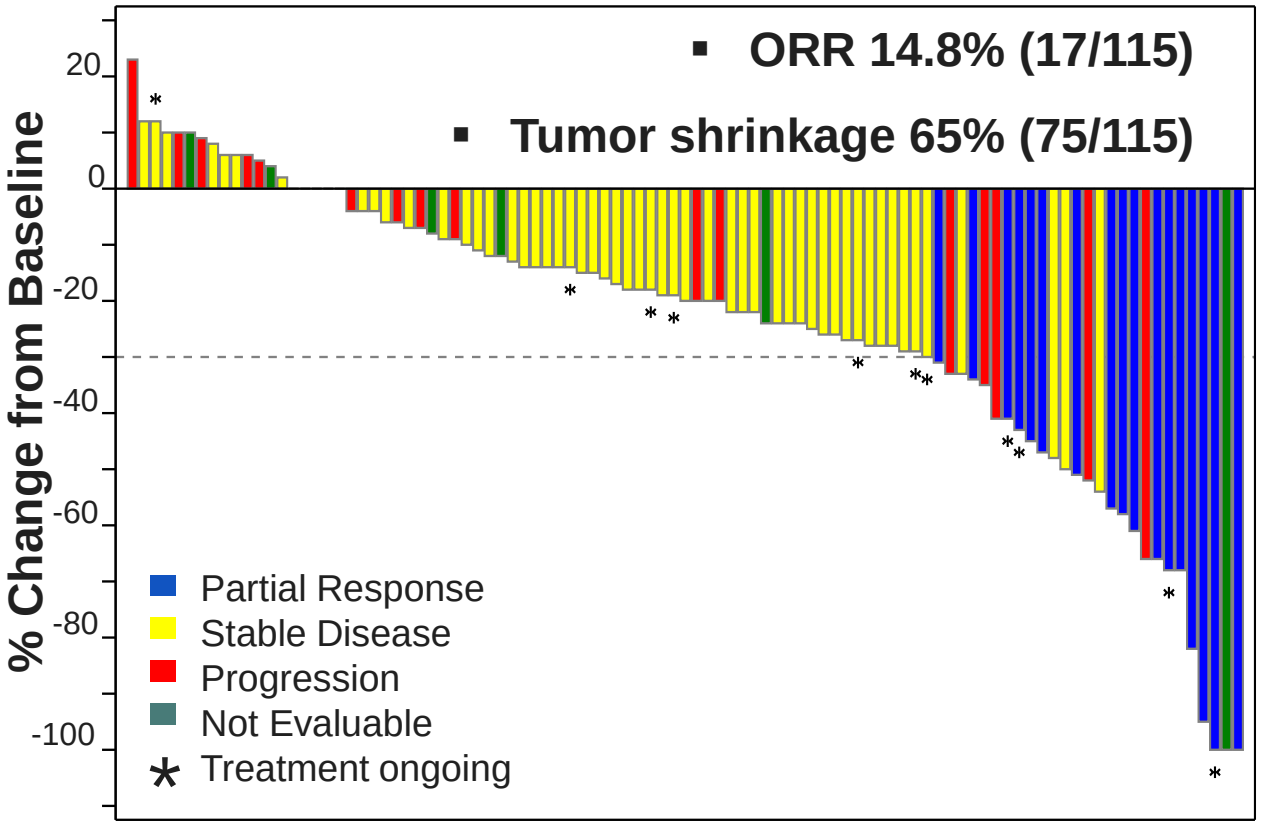
Characteristic		N (%)
Histopathological classification	Adenocarcinoma	112 (98)
	Squamous	3 (3)
	Mixed pathology	0
Disease stage at study entry	III	7 (6)
	IV	105 (91)
Brain metastases	None	103 (90)
	Present	12 (10)
ECOG PS	0	53 (46)
	1	62 (54)

Cohort 1 Results

Best Overall Response	Intent to treat (N=115) N (%)
Objective Response Rate (ORR) by independent review committee (IRC) 95% Confidence Interval	**17 (14.8%)** (8.9 - 22.6%)
Disease Control Rate (DCR=CR+PR+SD) 95% Confidence Interval	**79 (68.7%)** (59.4 - 77.0%)
Duration of Response, Median (months) 95% Confidence Interval	**7.4** (3.7, 9.7)
Progression-free Survival, Median (months) 95% Confidence Interval	**4.2** (3.7, 6.6)

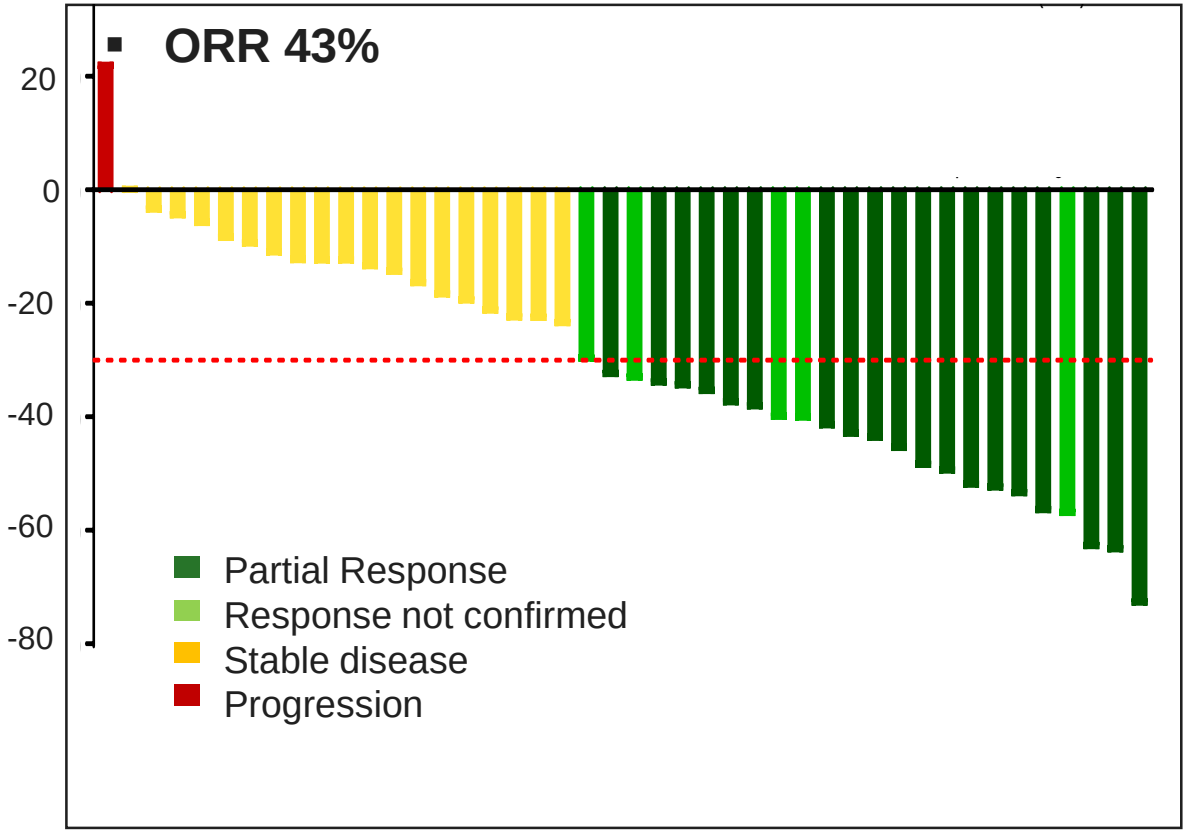
Efficacy: Tumor Size Reduction

Best change (%) in the sum target lesions
ZENITH20 cohort 1 (N=97)



Reviewed by Independent Review Committee (IRC)

MDACC single-center study (N=44)



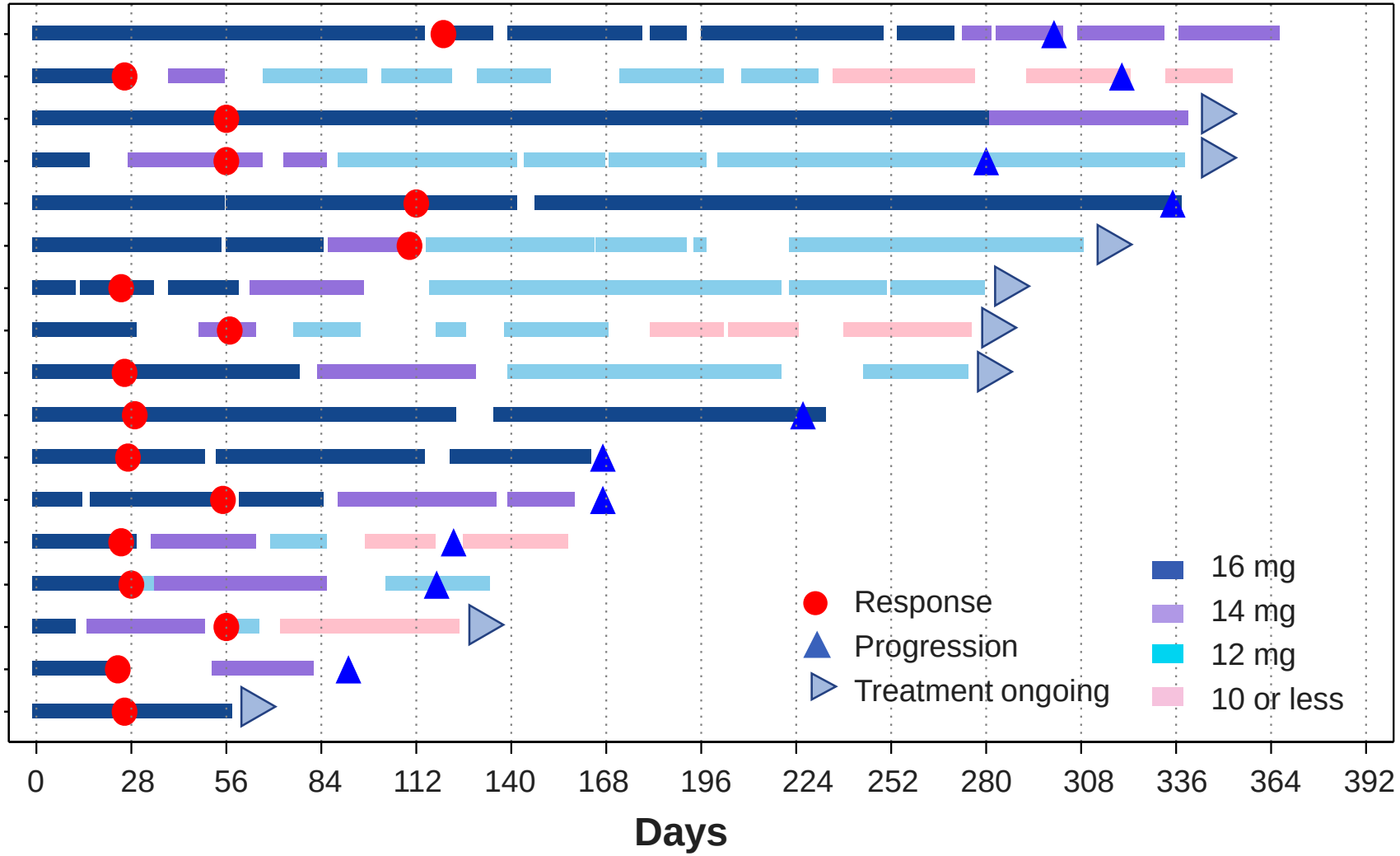
Elamin in preparation, Heymach WCLC 2018

Safety: Treatment-related Adverse Events

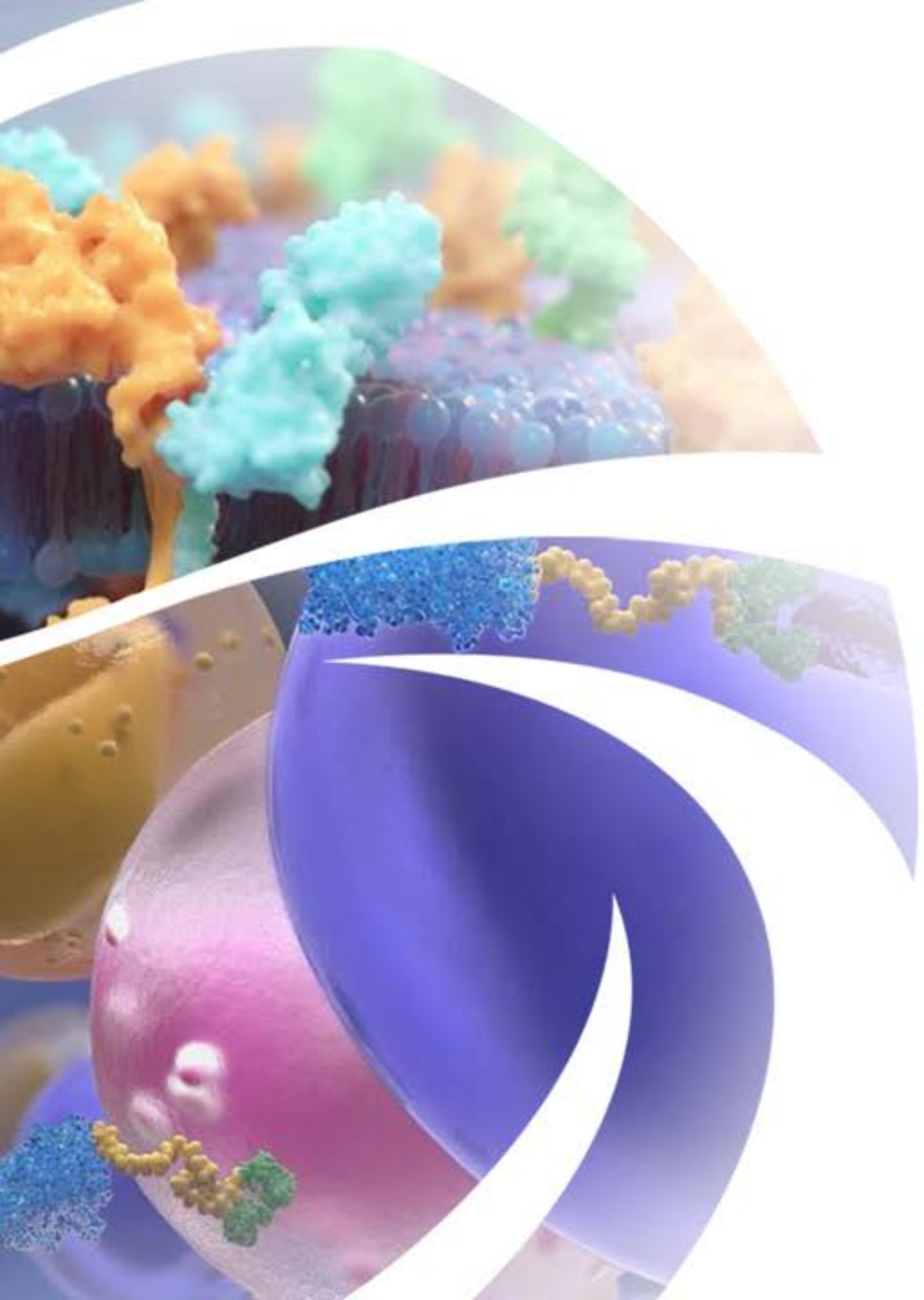
Treatment-related AE	N=115		
	Any Grade n (%)	Grade 3 n (%)	Grade 4 n (%)
Any TRAE	114 (99)	70 (61)	2 (2)
Diarrhea	91 (79)	29 (25)	1 (1)
Rash	69 (60)	32 (28)	0
Stomatitis	60 (52)	10 (9)	0
Paronychia	52 (45)	7 (6)	0
Nausea	44 (38)	3 (3)	0
Decreased appetite	36 (31)	2 (2)	0
Mucosal inflammation	34 (30)	8 (7)	0
Dry skin	33 (29)	3 (3)	0
Vomiting	33 (29)	1 (1)	0
Alopecia	31 (27)	0	0
Dermatitis acneiform	30 (26)	8 (7)	1 (1)
Fatigue	30 (26)	6 (5)	0
Pruritus	29 (25)	5 (4)	0

- Drug interruption rate 88%
- Dose reduction rate 68%
- Permanent discontinuation due to treatment-related AE = 12 (10%)
- No Grade 5 treatment related AE
- Most common treatment-related AEs (any grade) include:
  - Rash
  - Diarrhea
  - Stomatitis
  - Paronychia

Efficacy: Duration of Response



- Median duration of response: 7.4 months (95% CI 3.7,9.7)
- Responses occurred early and were durable



ZENITH20
Strategy and Next Steps

Francois Lebel, MD | Chief Medical Officer

April 28, 2020

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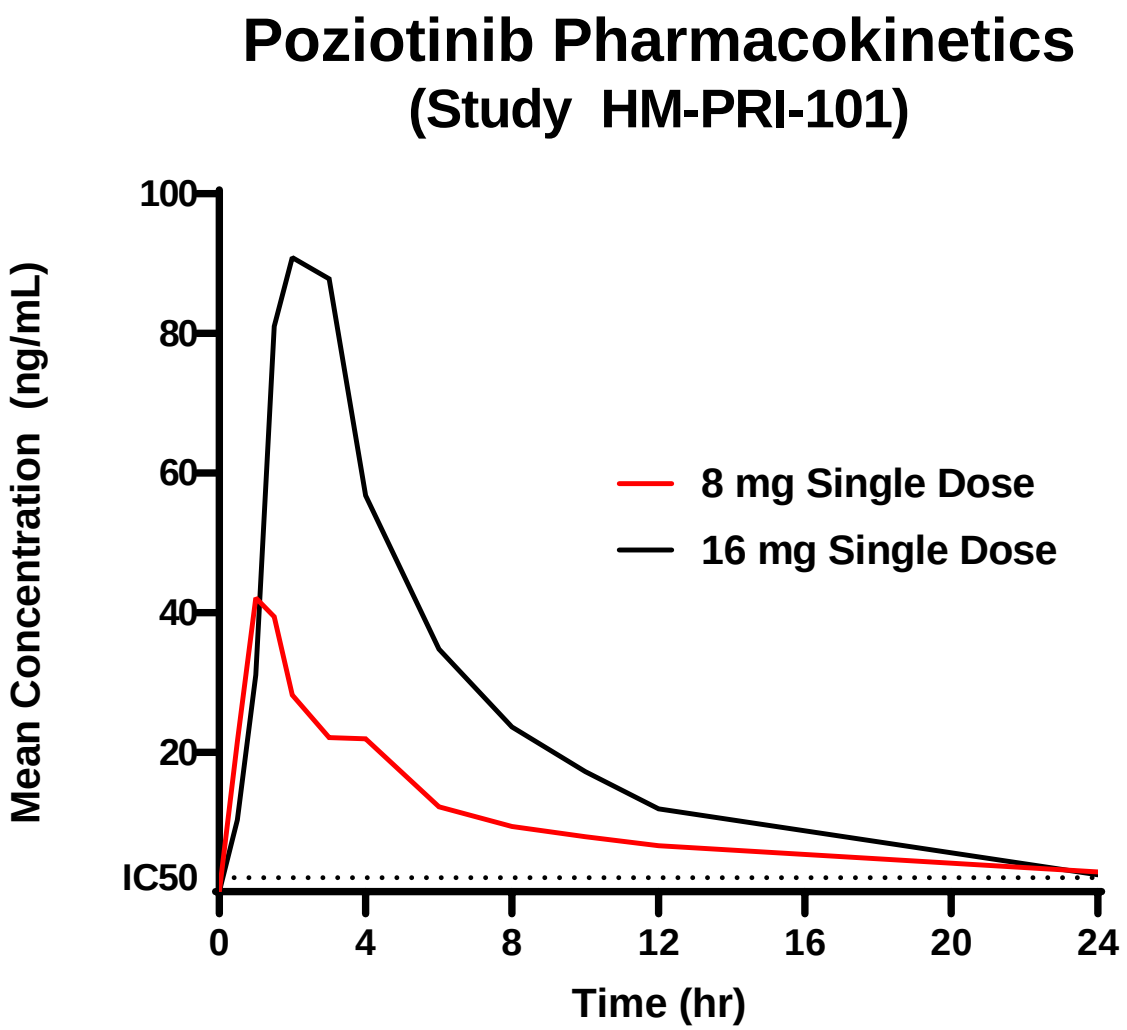
TKI Half-life and Dose

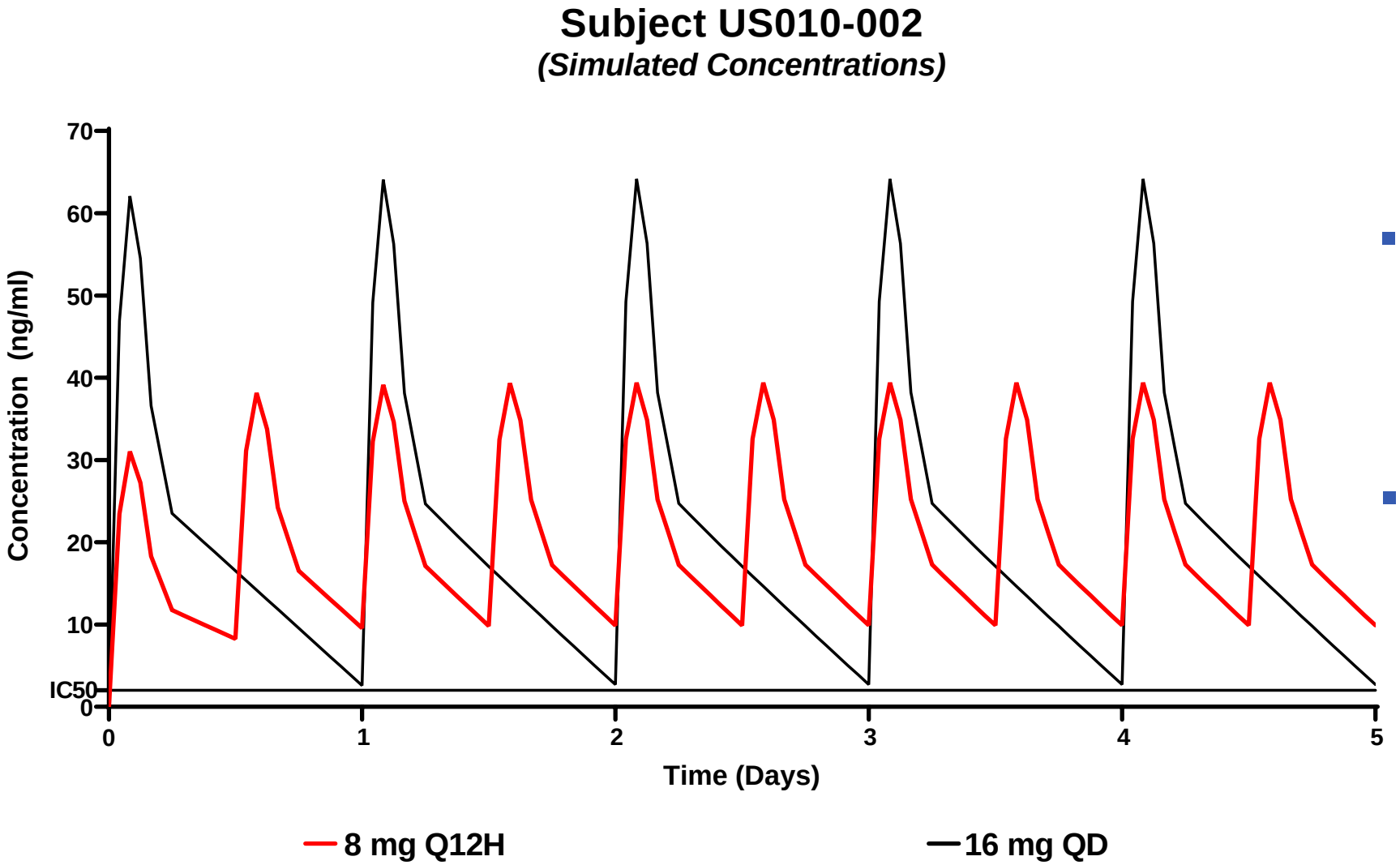
Test Article	Plasma 1/2 Life (hr)	Plasma Accumulation	Dose (mg)
Poziotinib	7.9	No	12-16 QD
TAK-788	16	No	160 QD
Osimertinib	48	Yes	80 QD
Neratinib	14.6	No	240 QD 6 tabs
Afatinib	37	Yes	20-50 QD

Poziotinib Pharmacokinetics



Parameter	Geometric Mean (Range)			
	8 mg Poziotinib		16 mg Poziotinib	
	Day 1	Day 14	Day 1	Day 14
C_{max} (ng/mL)	42.0 (35.5-49.5)	38.8 (29.6-53.9)	64.6 (45.8-90.9)	79.8 (49.6-160)
T_{max} (hr)	1.2 (1.0-1.6)	1.8 (1.0-4.0)	2.0 (1.0-3.0)	1.3 (1.0-2.0)
AUC_{0-24} (ng·hr/mL)	262.1 (189.2-379.6)	273.63 (207.2-358.2)	468.2 (267.1-668.3)	450.7 (258.1-904.4)
t½ (hr)	8.0 (5.9-9.4)	10.4 (8.3-13.2)	5.8 (4.85-7.4)	7.2 (4.58-9.9)
CL/F (L/hr)	27.2 (18.0-40.1)	24.3 (17.1-35.4)	32.5 (23.3-58.7)	35.1 (16.6-60.9)
Vz/F (L)	312.6 (240.3-373.7)	363.8 (327.4-424.5)	271.0 (162.9-416.6)	362.4 (145.0-536.6)

Simulated Poziotinib Plasma Concentrations 8 mg BID vs. 16 mg QD



- BID dosing
  - Decreases Cmax
  - Maintains Ctrough above IC50
- Pozi IC50 4nM (2ng/ml)-T790m

Highlights of Amendment

- Cohorts 1, 2, 3 are fully enrolled – No change to dosing
- Cohorts 4, 6, 7 – New patients on 8 mg BID dosing
- Cohort 5 – New patients being randomized to 10 mg, 6 or 8 mg BID dosing
- Minimize dose interruptions
- New recommendations for rash management
  - Intensified monitoring
  - Initiate steroids earlier

ZENITH20: Continued Enrollment with New Cohorts

NSCLC patients with EGFR or HER2 exon 20 insertions

Key Eligibility Criteria

- **NSCLC EGFR or HER2 exon20 insertions**
- Point mutations, including T790M, are not allowed
- Brain mets are allowed if stable

Osimertinib-resistant with EGFR mutations

Atypical EGFR or HER2 mutations

Cohort 1 **EGFR - previously treated**	Oral daily dose 28-day cycle
Cohort 2 HER2 - previously treated	16mg QD
Cohort 3 EGFR – treatment naive	
Cohort 4 HER2 – treatment naive	8mg BID
Cohort 5 EGFR or HER2 exon 20	Randomized to 10mg QD, 6mg BID, 8mg BID
Cohort 6 EGFR osimertinib failure	8mg BID
Cohort 7 Atypical EGFR or HER2 mutations	

Primary Endpoint

- Objective Response Rate (RECIST 1.1)

Secondary Endpoints

- Duration of response
- Disease control rate
- PFS (exploratory)
- Safety

Conclusions

- Poziotinib has demonstrated clinical activity in previously treated NSCLC patients with EGFR exon 20 insertions
- Dose reductions and interruptions due to AEs may have led to reduced efficacy
- PK modeling support BID dosing while reducing C_{max} and maintaining C_{trough} above IC_{50} level

Questions