

TYRA

Interim clinical proof-of-concept with
TYRA-300 in mUC (SURF301)

October 25, 2024

Today's participants and agenda



Todd Harris, PhD
CEO, TYRA



Doug Warner, MD
CMO, TYRA



Gary Steinberg, MD
Professor of Urology,
Dept. of Urology,
Rush University Medical Center

AGENDA

Todd Introduction

Doug Interim SURF301
TYRA-300 results

Gary Q&A: Perspective of
a leading Urologist

Disclaimers

FORWARD-LOOKING STATEMENTS AND MARKET DATA

We caution you that this presentation contains forward-looking statements. All statements other than statements of historical facts contained in this presentation, including statements regarding our business strategy, research and development plans, the anticipated timing and phase of development, costs, design and conduct of our ongoing and planned preclinical studies and clinical trials for our product candidates, the timing and likelihood of regulatory filings and approvals for our product candidates, the potential to develop product candidates and for them to be first-in-class, and the potential safety and therapeutic benefits of our product candidates, our ability to commercialize our product candidates, if approved, the pricing and reimbursement of our product candidates, if approved, the timing and likelihood of success, plans and objectives of management for future operations, and future results of anticipated product development efforts, are forward-looking statements. In some cases, you can identify forward-looking statements by terms such as "may," "will," "should," "expect," "plan," "anticipate," "could," "intend," "target," "project," "contemplates," "believes," "estimates," "predicts," "potential" or "continue" or the negative of these terms or other similar expressions. The inclusion of forward-looking statements should not be regarded as a representation by us that any of our plans will be achieved. Actual results may differ from those set forth in this presentation due to the risks and uncertainties inherent in our business, including, without limitation: interim results of a clinical trial are not necessarily indicative of final results and one or more of the clinical outcomes may materially change as patient enrollment continues, following more comprehensive reviews of the data, as follow-up on the outcome of any particular patient continues and as more patient or final data becomes available, including the risk that unconfirmed responses may not ultimately result in confirmed responses to treatment after follow-up evaluations; the potential for proof-of-concept results to fail to result in successful subsequent development of TYRA-300;

we are early in our development efforts, have only recently begun testing TYRA-300 and TYRA-200 for oncology in clinical trials and the approach we are taking to discover and develop drugs based on our SNAP platform is novel and unproven and it may never lead to product candidates that are successful in clinical development or approved products of commercial value; potential delays in the commencement, enrollment, data readouts, and completion of preclinical studies and clinical trials; results from preclinical studies or early clinical trials not necessarily being predictive of future results; our dependence on third parties in connection with manufacturing, research and preclinical testing; we may expend our limited resources to pursue a particular product candidate and/or indication and fail to capitalize on product candidates or indications with greater development or commercial potential; acceptance by the FDA of INDs or of similar regulatory submissions by comparable foreign regulatory authorities for the conduct of clinical trials of TYRA-300 in pediatric achondroplasia or hypochondroplasia; an accelerated development or approval pathway may not be available for TYRA-300 or other product candidates and any such pathway may not lead to a faster development process; later developments with the FDA may be inconsistent with the minutes from our prior meetings, including with respect to the design of our planned Phase 2 study of TYRA-300 in ACH; unexpected adverse side effects or inadequate efficacy of our product candidates that may limit their development, regulatory approval, and/or commercialization; the potential for our programs and prospects to be negatively impacted by developments relating to our competitors, including the results of studies or regulatory determinations relating to our

competitors; unfavorable results from preclinical studies; we may not realize the benefits (i) associated with orphan drug designation, including that orphan drug exclusivity may not effectively protect a product from competition and that such exclusivity may not be maintained or (ii) from the rare pediatric disease designation, including potential to receive a Priority Review Voucher (PRV) or derive any value therefrom; regulatory developments in the United States and foreign countries; our ability to obtain and maintain intellectual property protection for our product candidates and proprietary technologies; and other risks described in our prior filings with the Securities and Exchange Commission (SEC), including under the heading "Risk Factors" in our annual report on Form 10-K and any subsequent filings with the SEC. You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof, and we undertake no obligation to update such statements to reflect events that occur or circumstances that exist after the date hereof. All forward-looking statements are qualified in their entirety by this cautionary statement, which is made under the safe harbor provisions of the Private Securities Litigation Reform Act of 1995.

This presentation also contains estimates and other statistical data made by independent parties and by us relating to market size and growth and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. In addition, projections, assumptions, and estimates of our future performance and the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk. These and other factors could cause results to differ materially from those expressed in the estimates made by the independent parties and by us.

Our expertise in FGFR biology creates a differentiated pipeline

GENETIC CONDITIONS	Estimated Annual US Addressable ¹	Phase						
		Discovery	IND-Enabling	1	2	3	Anticipated Milestone	
FGFR3 ^{ACH} : TYRA-300	~3K	—————●—————		Data from FGFR3 ^{ONC}▶		Initiate Ph 2 study

Potentially leading to additional skeletal dysplasias, including FGFR3-related conditions (HCH, SHOX), and pediatric short stature

ONCOLOGY

FGFR3 ^{ONC} : TYRA-300	~40K	—————●—————						Further QD dose optimization
FGFR2 ^{ONC} : TYRA-200	~5.5K	—————●—————						Complete Ph1
FGFR4/3 ^{ONC} : TYRA-430	~9K	—————●—————						Dose first patient

TYRA retains an active FGFR3 discovery program.

1. Represents FGFR3/FGFR2/FGF19+ incidence and relapses for TYRA300/200/430, prevalence for ACH

TYRA-300 is the world's first oral, selective FGFR3 inhibitor with the potential to deliver benefit to cancer patients with a tolerable safety profile

	BENCHMARK ¹	READOUT
 ACTIVITY	On par with erdafitinib label in FGFR3+ mUC patients at active dose levels	54.5% (6/11) confirmed PRs vs. 35.3% ORR erdafitinib label
PK/PD		
SAFETY		

1. This comparison is solely based on BALVERSA® (erdafitinib) prescribing information as of January 2024 and not based on any head-to-head clinical trials. Cross-study comparisons are inherently limited and may suggest misleading similarities and differences. The values shown in the cross-study comparisons are directional and may not be directly comparable.

TYRA-300 is the world's first oral, selective FGFR3 inhibitor with the potential to deliver benefit to cancer patients with a tolerable safety profile

SURF ³⁰¹	ACTIVITY	BENCHMARK ¹	READOUT
PK/PD	Dose-dependent activity	Anti-tumor activity observed in all FGFR3+ mUC ≥90 mg QD	54.5% (6/11) confirmed PRs vs. 35.3% ORR erdafitinib label
SAFETY	On par with erdafitinib label in FGFR3+ mUC patients at active dose levels		

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PK/PD	Dose-dependent activity	Anti-tumor activity observed in all FGFR3+ mUC ≥90 mg QD
SAFETY	Safety profile with improved tolerability in FGFR1/2/4-driven toxicities compared to pan-FGFRis	Generally well-tolerated with infrequent FGFR2- and FGFR1-associated toxicities

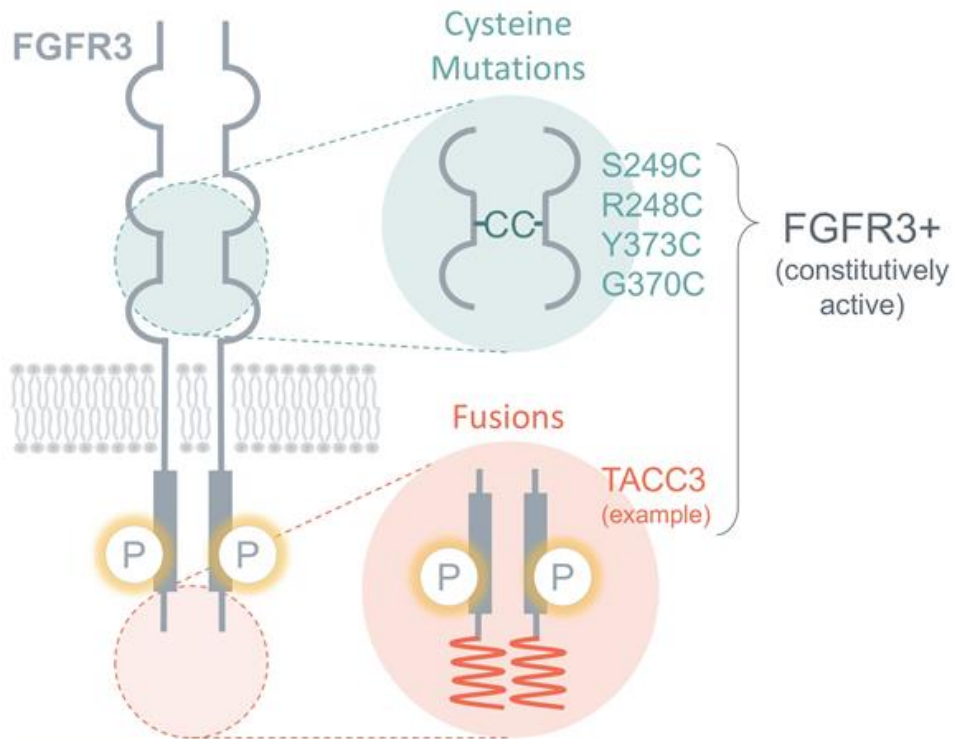
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SURF³**301**

INTERIM PHASE 1 RESULTS
ENA 2024

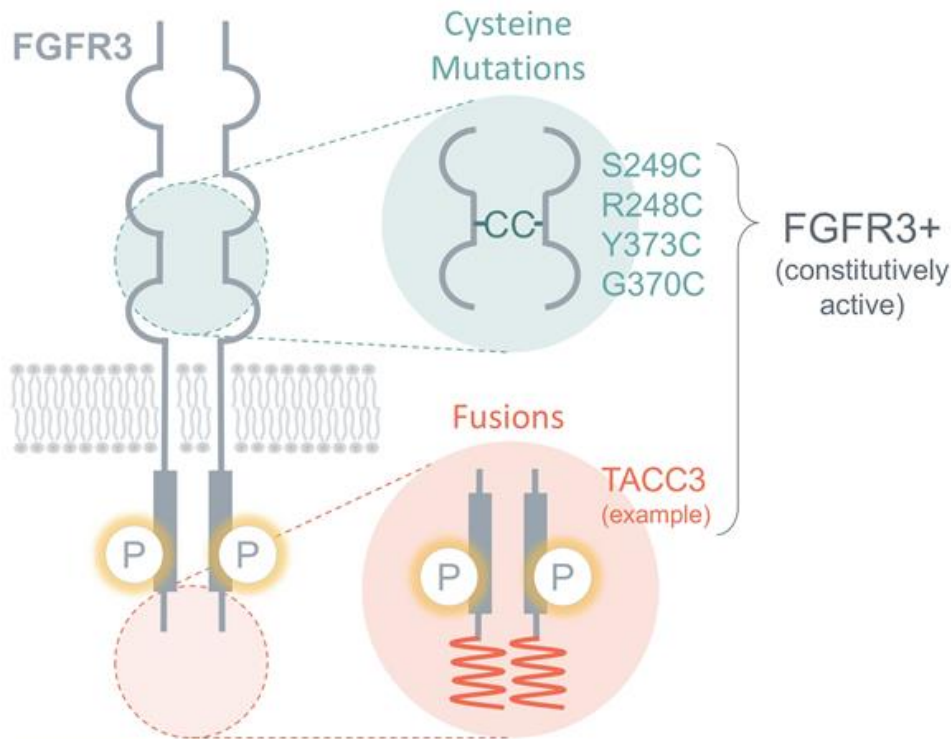
FGFR3 oncogenic alterations are common in bladder cancer



Abbreviations: IR, Intermediate Risk; HR, High Risk

1. Weickhardt 2022 2. Mayr, 2022; Kacew, 2020; Knowles, 2020 3. BALVERSA® (erdafitinib) prescribing information 01/2024; BLC3001 Cohort 1 trial data 4. Daneshmand, 2023 (SUO) 5. Catto, 2023 (SUO) 6. Lyou, 2022 7. Cha, 2020 (ASCO GU) 8. Necchi, 2023; represents ORR for continuous dosing cohort

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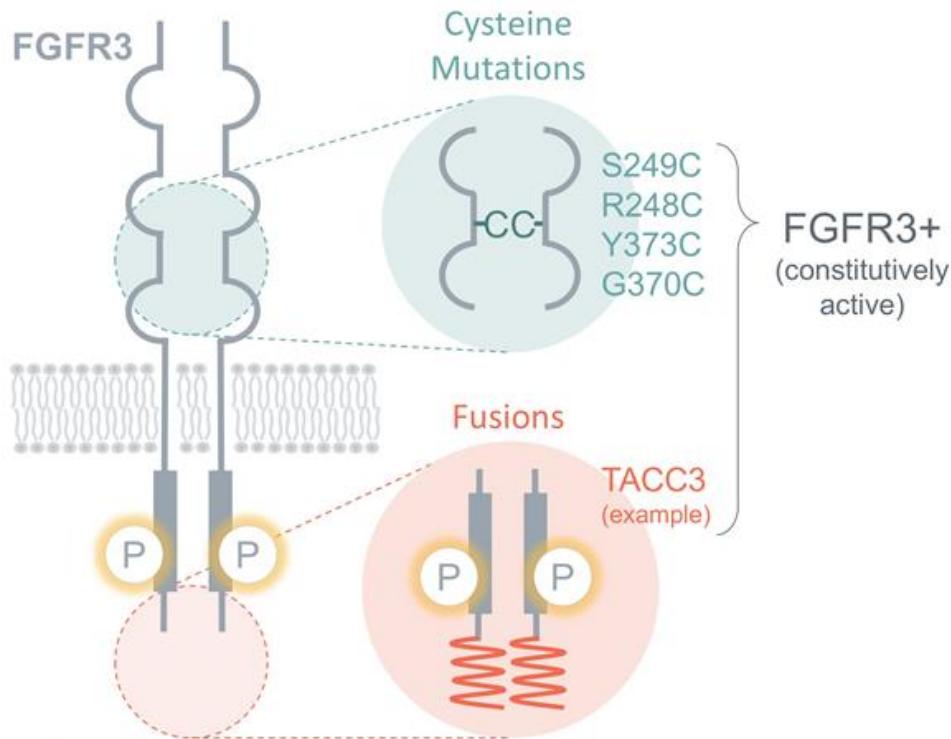


mUC	
FGFR3+	10–20% ¹
Oral erdafitinib	35.3% ORR, 12.1mo OS ³ (n=136)
infigratinib	24% ORR ⁶ (n=54)
pemigatinib	23% ORR ⁸ (n=103)

Abbreviations: IR, Intermediate Risk; HR, High Risk

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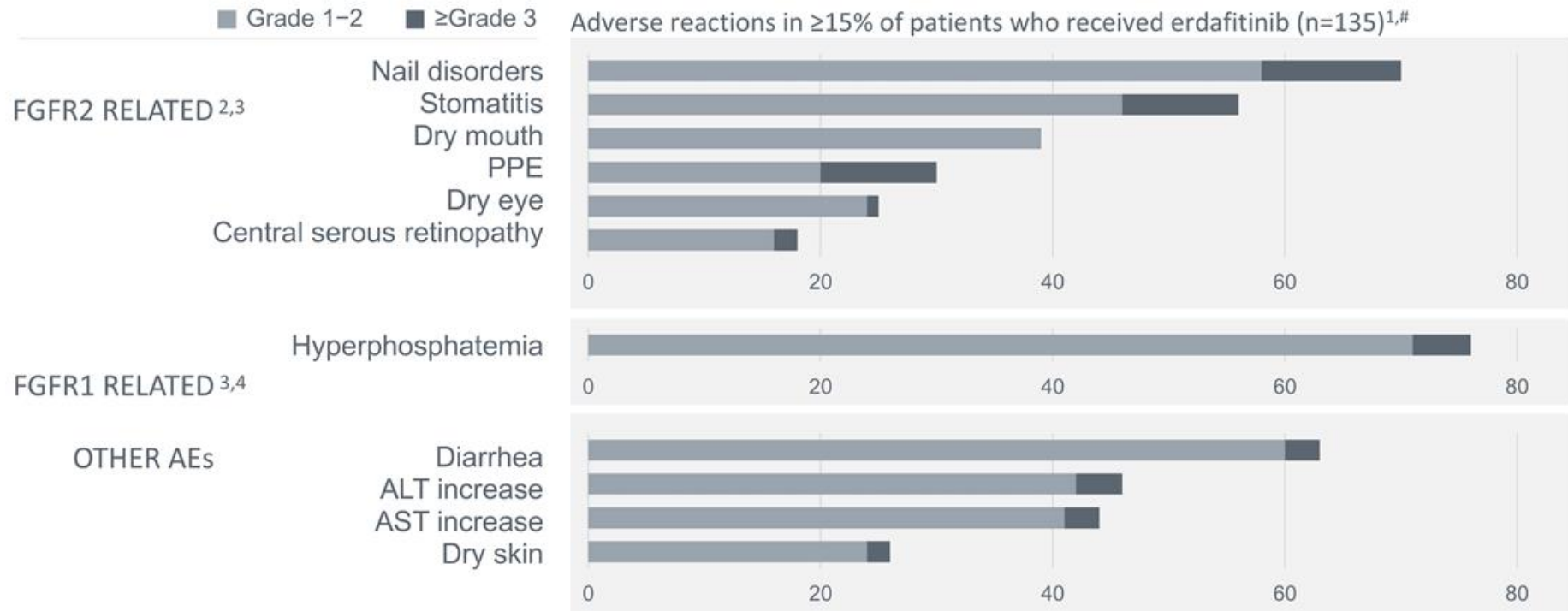


	mUC	NMIBC
FGFR3+	10–20% ¹	40–80% ²
Oral erdafitinib	35.3% ORR, 12.1mo OS ³ (n=136)	IR: 83% CR ⁴ (n=18) HR(Cis): 73% CR ⁵ (n=11)
infigratinib	24% ORR ⁶ (n=54)	HR (Pap): 75% CR ⁷ (n=4)
pemigatinib	23% ORR ⁸ (n=103)	

Abbreviations: IR, Intermediate Risk; HR, High Risk

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Pan FGFR inhibition is associated with key on-target toxicities



¹Adapted from: Erdafitinib tablets, for oral use. Prescribing information 01/2024. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/212018s007s008s009tbl.pdf. Accessed 06 October 2024. ²Lacouture ME et al. Oncologist. 2021. ³Subbiah V, Verstovsek S. Cell Rep Med. 2023. ⁴Kommalapati A, et al. Cancers. 2021. [#]Study BLC3001

Adverse reactions have occurred requiring dosage modifications of erdafitinib

Adverse reactions resulting in dose adjustments in patients who received erdafitinib (n=135)¹

INTERRUPTION

72%

Nail disorders	22
Stomatitis	19
Eye disorders	16
PPE	15
Diarrhea	10
Hyperphosphatemia	7
Increased AST	6
Increased ALT	5

REDUCTION

69%

Nail disorders	27
Stomatitis	19
Eye disorders	17
PPE	12
Diarrhea	7
Dry mouth	4.4
Hyperphosphatemia	4.4

DISCONTINUATION

14%

1. BALVERSA (erdafitinib) prescribing information 01/2024, BLC3001 Cohort 1 data. Adverse reactions leading to dosage interruptions or reductions of erdafitinib in >4% of patients.

TYRA-300 is a potential first-in-class, highly selective FGFR3 inhibitor

Selectivity observed for TYRA-300 vs. approved or late-stage clinical compounds: *in vitro* Ba/F3 Cellular IC₅₀ (nM)



	E	F	P	I
FGFR1	4.2x	4.9x	2.4x	2.2x
FGFR2	1.4x	1.3x	0.8x	0.8x
FGFR4	14x	7.6x	27x	67x

All experiments conducted under identical conditions, tested in duplicate.

Our Phase 1 explored QD* dose escalation and expansion

Illustrative

**Dose
Escalation**

PART A
(all comers)
Dose QD*

All solid tumor types¹
FGFR+/-

SURF₃₀₁

**Dose
Expansion**

PART B
(FGFR3+ only)
Dose QD

Solid tumors with focus on mUC¹
FGFR3+ only

*1x daily

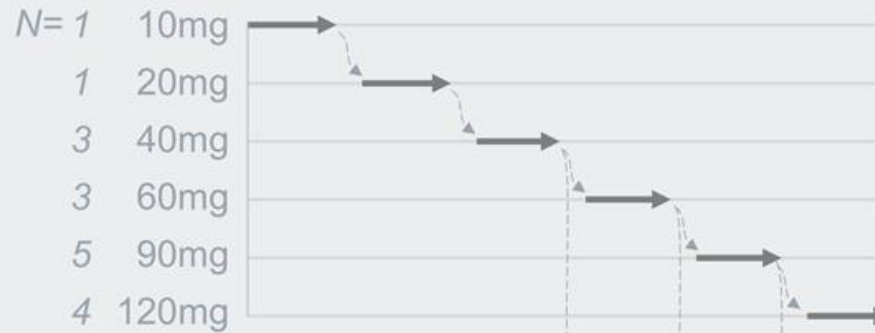
1. Previously treated patients, including FGFRi, allowed

We dose escalated to 120mg QD and then expanded up to 90mg

Illustrative

Dose
Escalation

PART A
(all comers)
Dose QD*



SURF₃₀₁

Dose
Expansion

PART B
(FGFR3+only)
Dose QD



*1x daily

The study population was older and heavily pre-treated

n=41		
MEDIAN AGE	(range 34–84)	66 (yrs)
		n (%)
SEX AT BIRTH	Male	30 (73)
ECOG PS	0	14 (34)
	1	27 (66)
FGFR3 ALTERATION	Mutation	17 (41)
	Fusion	15 (37)
	None	10 (24)

		n (%)
TUMOR TYPE	mUC	25 (61)
	Lung	3 (7)
	Head and Neck	4 (10)
	Other	9 (22)
PRIOR LINES OF THERAPY	0	5 (12)
	1	7 (17)
	2	11 (27)
	≥3	18 (44)

Abbreviations: mUC, metastatic urothelial cancer
Safety analysis set, n=41

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PRIOR LINES OF THERAPY	0	5 (12)
	1	7 (17)
	2	11 (27)
	≥3	18 (44)

76%

of mUC patients
had ≥3 prior lines
of therapy

Abbreviations: mUC, metastatic urothelial cancer
Safety analysis set, n=41

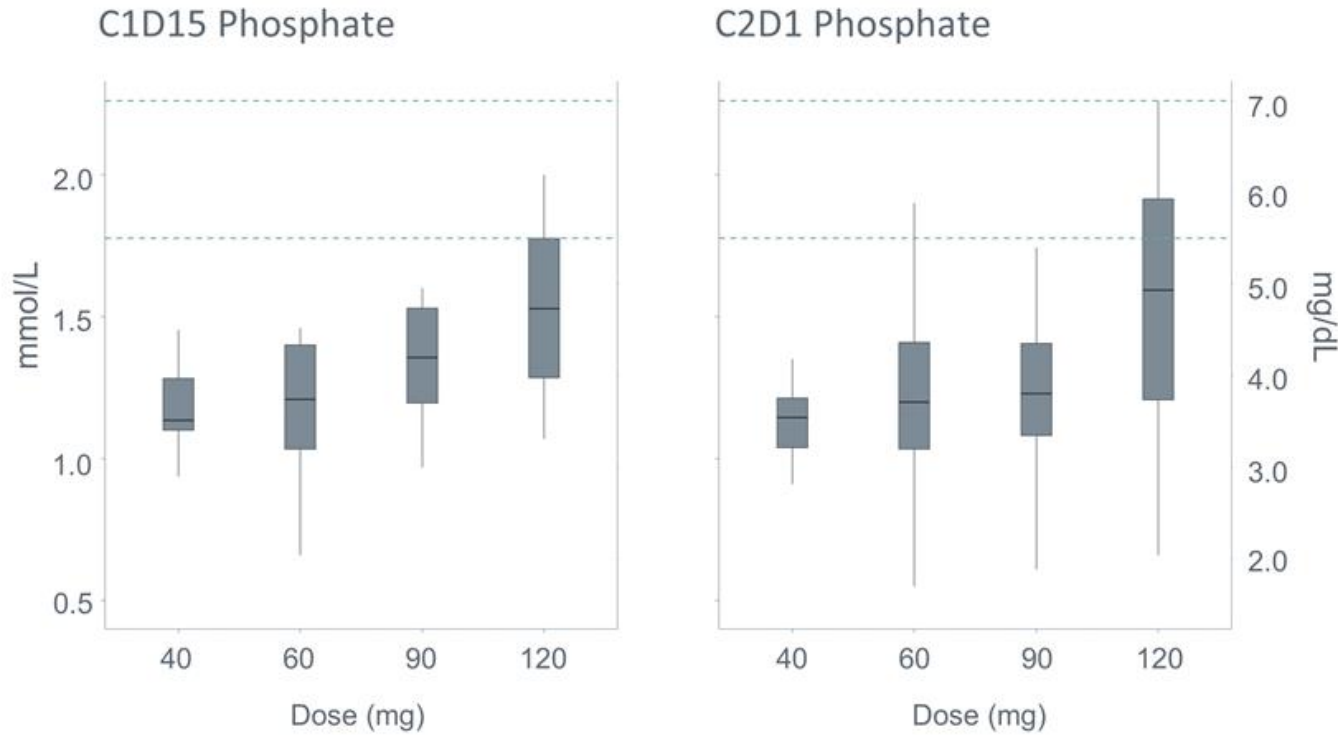
Preliminary data suggests TYRA-300 is generally well tolerated

n=41	Any Grade	≥ Grade 3
Any TRAEs, n (%)	32 (78)	8 (20)
TRAEs in >10% of participants, n(%)		
ALT increase [#]	10 (24)	2 (5)
Diarrhea*	9 (22)	1 (2)
Dry mouth	9 (22)	
AST increase	8 (20)	1 (2)
Dry skin	6 (15)	
Fatigue	5 (12)	

[#]Drug-related discontinuation, Grade 3 ALT elevation 90 mg QD; *DLT, Grade 3 diarrhea 90 mg QD
 Abbreviations: TRAE, treatment-related adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase;
 DLT, dose-limiting toxicity; SAE, serious adverse event
 Safety analysis set, n=41

- 1** DLT _____ 90 mg QD, Gr. 3 diarrhea*
- 1** Drug-related discontinuation _____ 90 mg QD, Gr. 3 ALT elevation[#]
- 4** Related SAEs _____ Related to TYRA-300
- 0** ≥Grade 4 SAE _____ No drug-related events leading to death

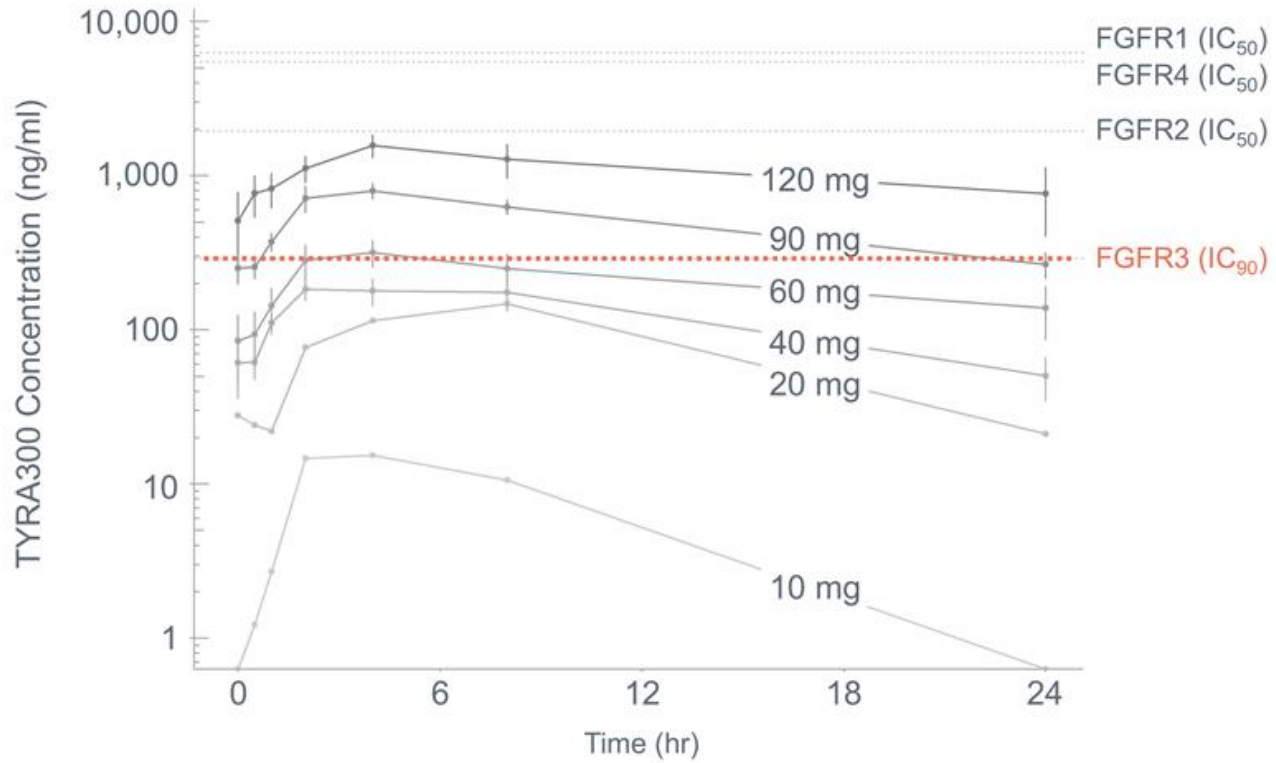
Minimal changes in phosphate at ≤ 90 mg QD observed



Phosphate binder was used to manage treatment-related hyperphosphatemia in one patient (90 mg QD).

Minimal impact in phosphate at ≤ 90 mg QD. Dashed lines denote 5.5 and 7 mg/dL used by Lorient et al. where 5.5- 6.9 mg/dL was defined as Grade 1 and 7.0-8.9 mg/dL as Grade 2.

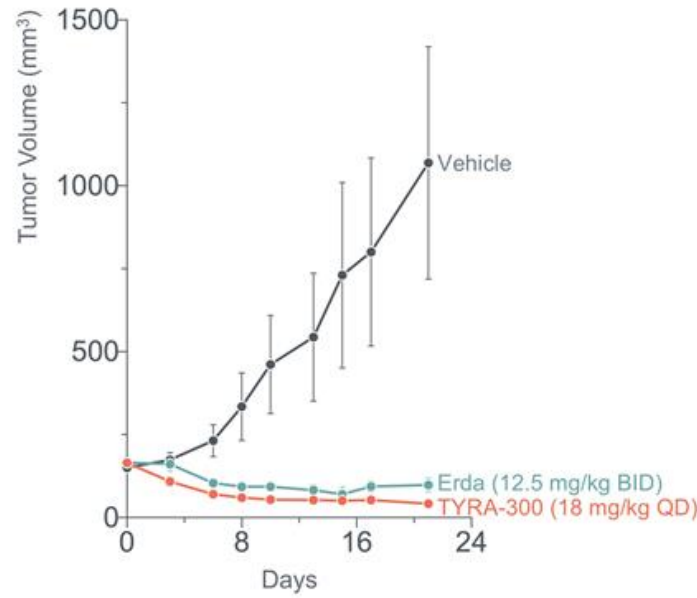
Exposure at doses ≥ 90 mg exceeded FGFR3 IC_{90} target coverage



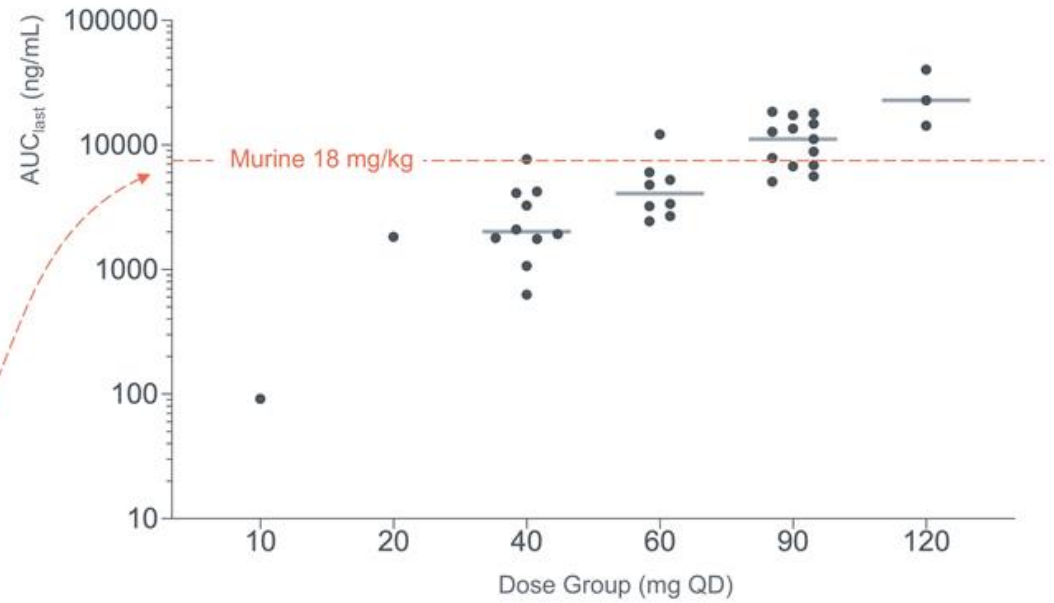
Dose (mg)	N (C1D15)	AUC (ng*h/mL)	Ratio
120	3	23,578	2.5x
90	13	10,300	
60	8	4,360	2.4x
40	10	2,270	
20	1	1,830	2.5x
10	1	91.5	

Predicted exposure was achieved in human doses ≥ 90 mg QD

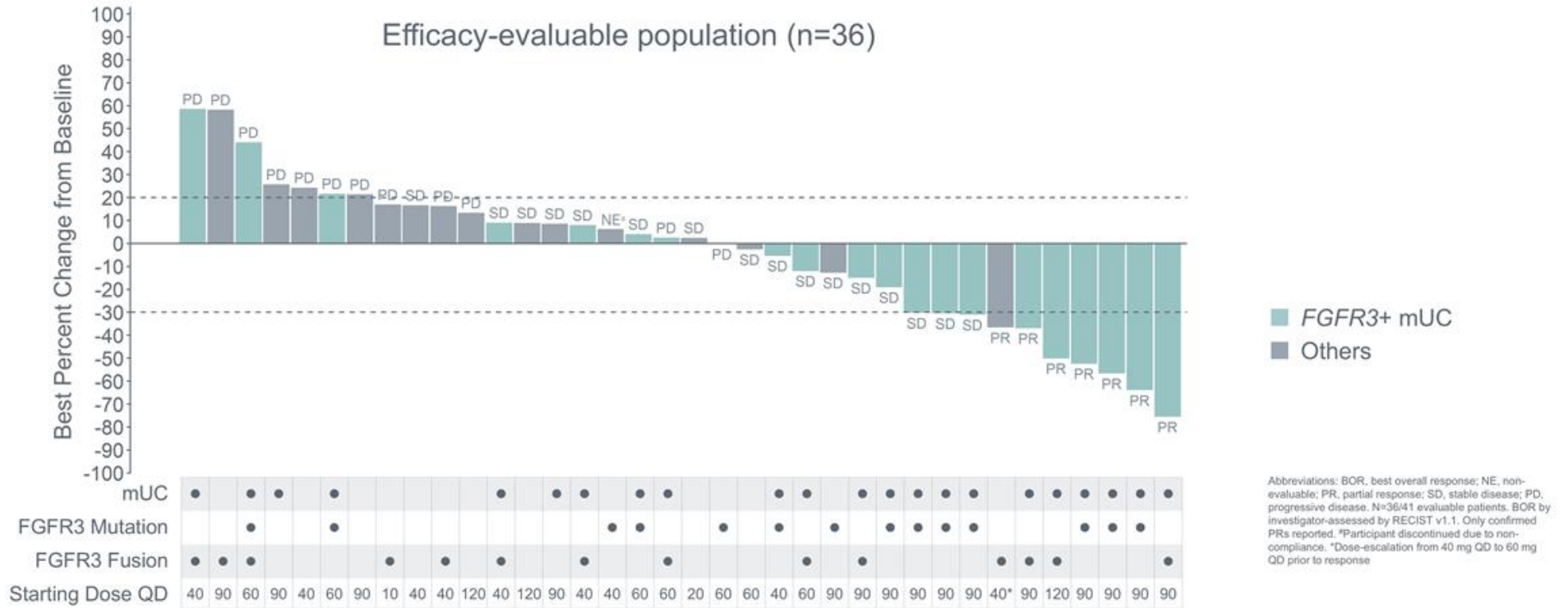
FGFR3+ UM-UC-14 Xenograft



Individual Steady State AUCs in Patients



Radiographic tumor response assessment in all evaluable patients



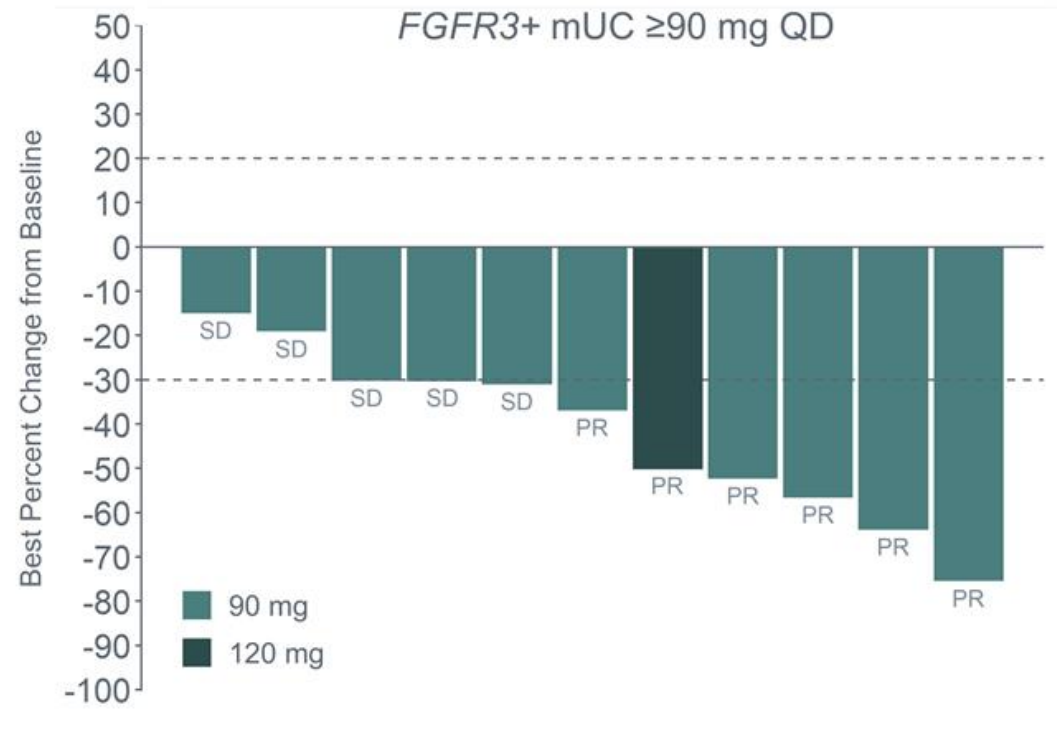
Anti-tumor activity observed in all *FGFR3*+ mUC ≥ 90 mg QD

Investigator-assessed radiographic BOR by RECIST v1.1 (n=11)

6 (54.5%) confirmed PRs at ≥ 90 mg QD (n=11)

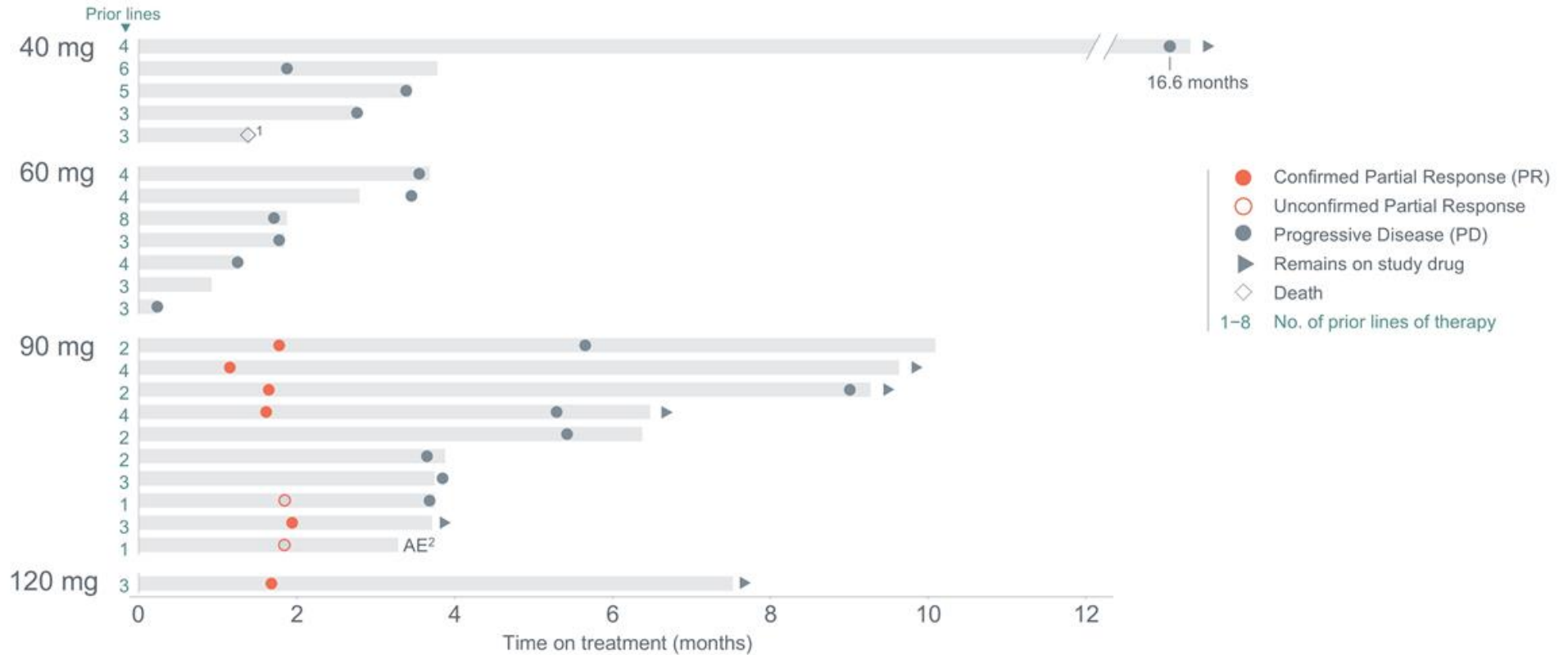
- 5 confirmed PRs at 90 mg QD (n=10)
- 1 confirmed PR at 120 mg QD (n=1)

100% Disease Control Rate



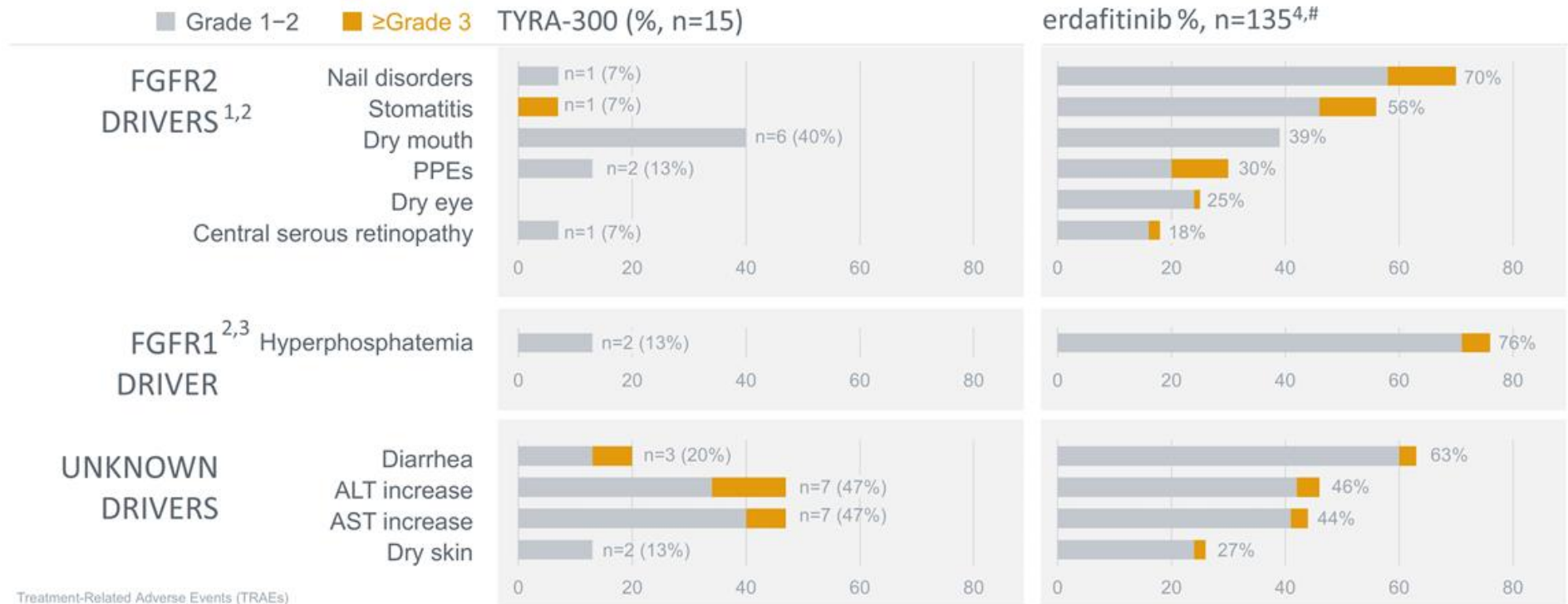
Abbreviations: BOR, best overall response; CR, complete response; PR, partial response; SD, stable disease. Only confirmed PRs reported.
Disease Control Rate: CR+PR+SD

Time on treatment for target population, *FGFR3+* mUC



1. Death unrelated to study drug (Respiratory Syncytial Virus)
 2. AE refers to adverse event

At 90mg QD, improved tolerability observed compared to erdafitinib



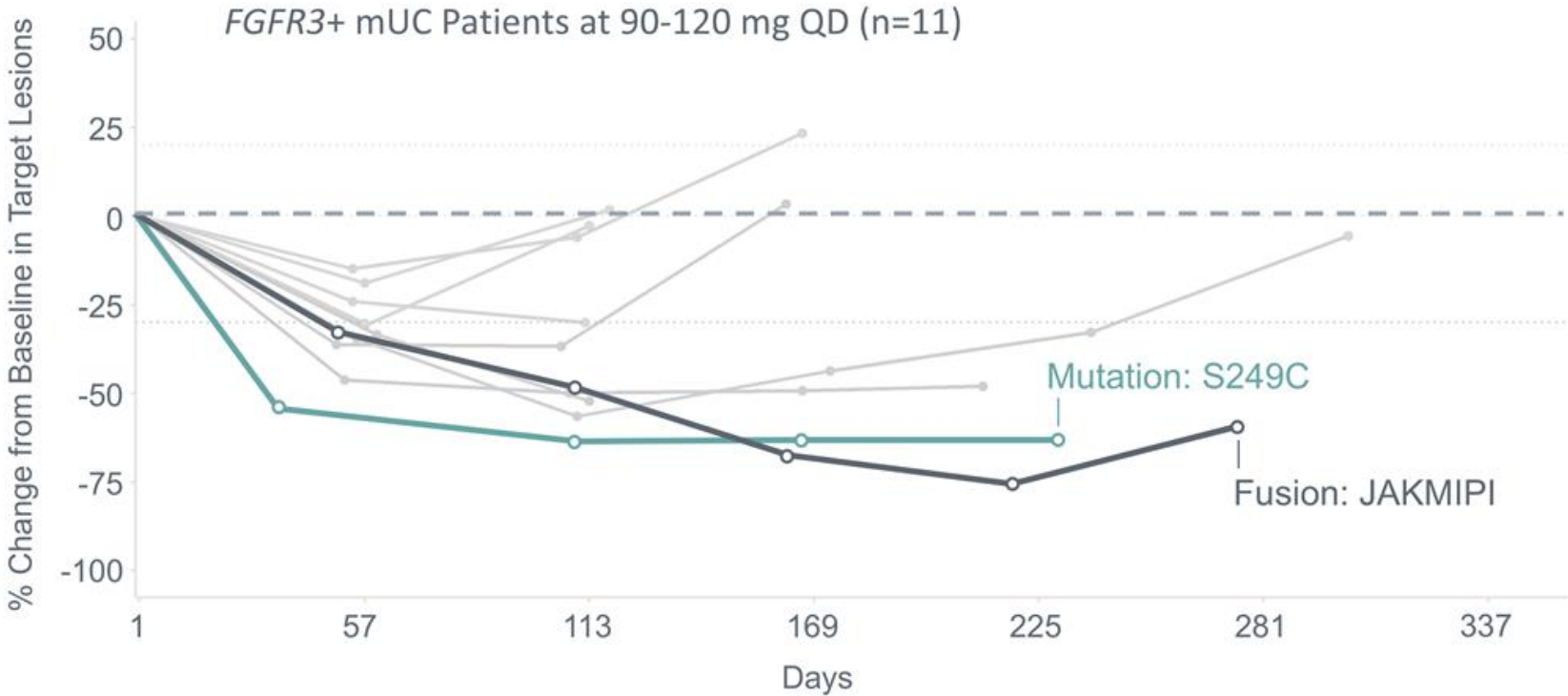
Treatment-Related Adverse Events (TRAEs)

¹Lacouture ME, et al. *Oncologist*. 2021. ²Subbiah V, Versteck S. *Cell Rep Med*. 2023. ³Kommalapati A, et al. *Cancers*. 2021. ⁴BALVERSA® (erdafitinib) prescribing information 01/2024; [#]BLC3001 Cohort 1 data, Adverse reactions leading to dosage interruptions or reductions of erdafitinib in >4% of patients

Results are preliminary based on the emerging data from the ongoing Phase 1 portion of the SURF301 study

90 mg QD: Dose reduction, n = 4; Discontinuation, n = 1

Radiographic regression seen at first imaging



Based on Investigator Assessment; RECIST v 1.1

Case study: mUC with activating *FGFR3*^{S249C} mutation

Mutation

Age/sex: 84-year-old female

Alteration: *FGFR3* S249C

Prior tx: 4 prior lines

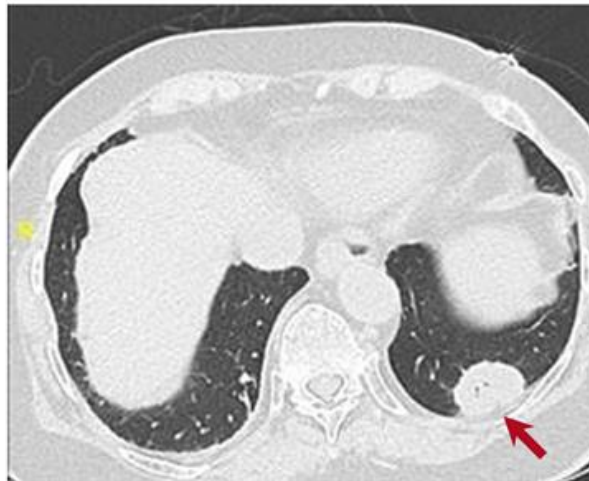
Target lesions: Lung

NTL: Lung, bone

BOR: -64% (cPR)

Treatment: 90 mg QD, 11 mo.*

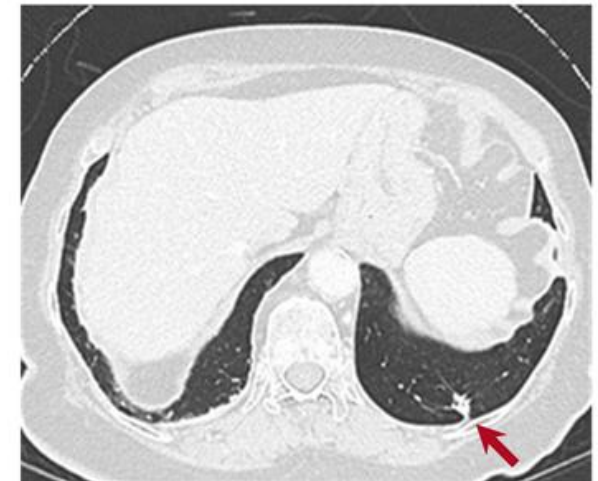
SEPT 25, 2023



Baseline

LUNG TARGET LESION

JAN 15, 2024



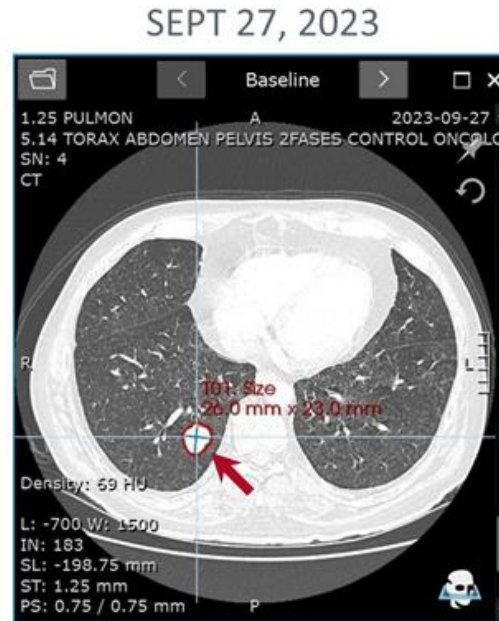
Confirmed PR

* Treatment ongoing at time of data cut
BOR: Best Overall Response; cPR: Confirmed Partial Response; NTL: Non-Target Lesion; tx: Therapy

Case study: mUC with activating *FGFR3-JAKMIPI* fusion

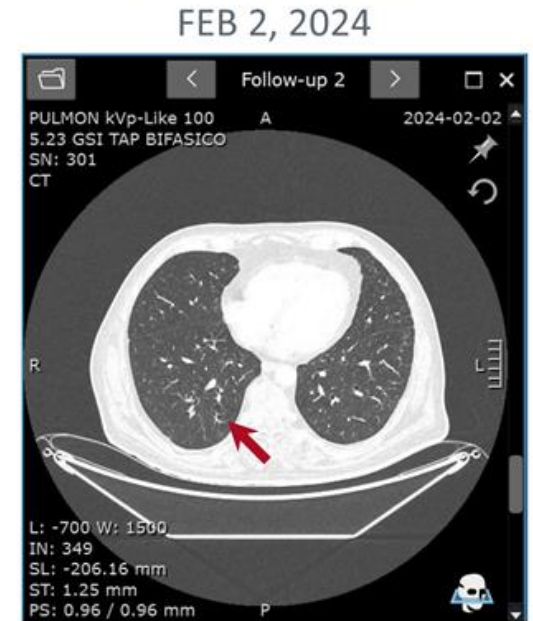
— Fusion —

Age/sex:	64-year-old male
Alteration:	FGFR3 JAKMIPI
Prior tx:	2 prior lines
Target lesions:	lung (x2), LN (x2)
NTL:	lung (x2) and LN (x2)
BOR:	-75% (cPR)
Treatment:	90 mg QD, 11 mo.*



Baseline

— LUNG TARGET LESION —



Confirmed PR

* Treatment ongoing at time of data cut
 BOR: Best Overall Response; cPR: Confirmed Partial Response; NTL: Non-Target Lesion; tx: Therapy

Interim clinical proof-of-concept established with TYRA-300 in mUC

1

Preliminary data from SURF301 suggest TYRA-300 to be generally well-tolerated, with infrequent FGFR2- and FGFR1-associated toxicities.

2

TYRA-300 plasma concentrations indicate adequate target coverage at ≥ 90 mg QD; further pharmacokinetic characterization is ongoing.

3

Preliminary anti-tumor activity of TYRA-300 in heavily pre-treated patients is encouraging, especially at doses ≥ 90 mg QD.

Phase 1 is ongoing and the MTD was not reached; the optimal dose is yet to be determined. Emerging data warrants continued development in mUC, prioritizing QD dosing.



LOOKING AHEAD: TYRA-300

mUC Improved toxicity profile

NMIBC ... Patient-friendly oral

ACH Differentiated efficacy

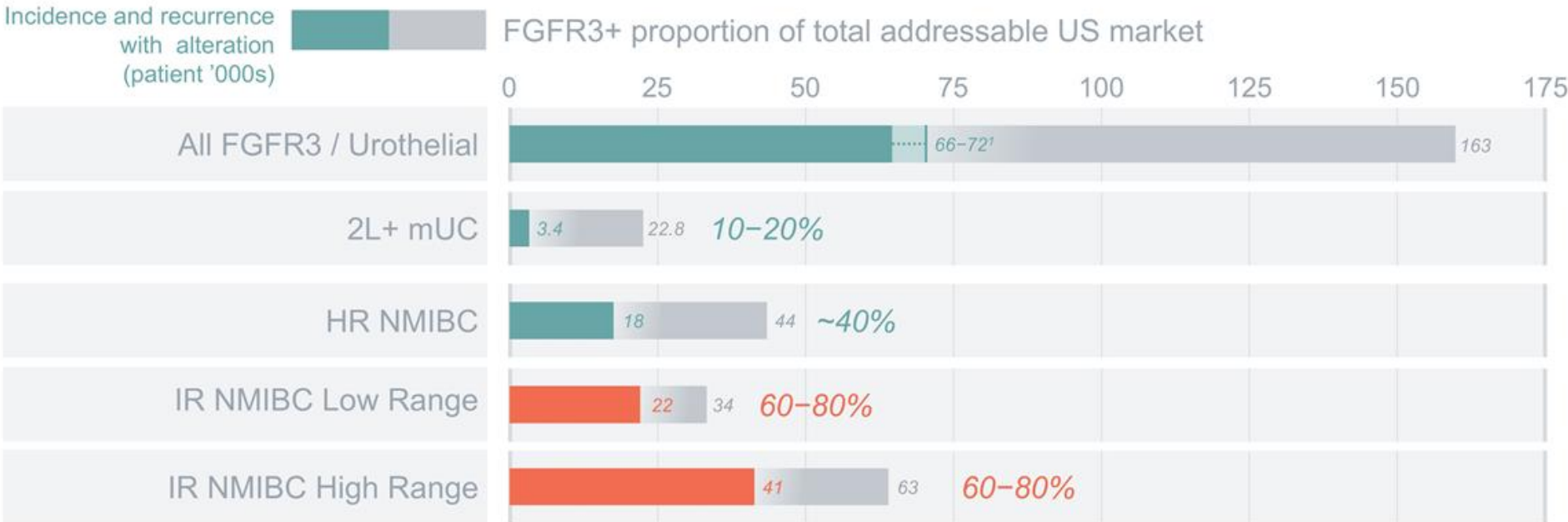
Attractive market opportunities for TYRA-300

	2L+ mUC	NMIBC	ACH
Total addressable (incident and recurrent) FGFR3+ Market Size	US: ~3.4K	IR US: ~22-41K	US: ~3K Global: ~20K
Unmet Needs	Less FGFR1/2/4-related and other toxicities	Reduction in recurrence Oral administration vs TURBT + chemotherapy	Differentiated efficacy Oral administration vs daily injection
SURF301 Dataset Read Through	Improved tolerability	Generally tolerable at exposures ~2/3 ¹ of the mUC dose	Generally tolerable at <50% ² of the mUC dose

1. Estimated based on 6mg oral erdafitinib dose studied in THOR-2 for NMIBC

2. Estimated based on infigratinib preclinical 2mg/kg model demonstrating efficacy at a dose translating to <50% of dose tested in mUC

High FGFR3+ rate drives an outsized opportunity in IR NMIBC



1. All FGFR3/Urothelial includes Low Risk NMIBC, which is not included in addressable population lines below
 FGFR3+ Rate Sources: Knowles, 2020; Mayr, 2022; Kacew, 2020; Weickhardt 2022; MIBC, mUC; MIBC and mUC Epidemiology Source: DR/Decision Resources LLC 2023 Epidemiology Figures
 NMIBC Epidemiology Source: CancerMPact® Patient Metrics, Oracle Life Sciences. Available from cancermpact.isapps.oracle.com. Accessed 18 Sep 2024; Low range driven by Ravvaz, 2019; Caputo, 2020; Check, 2019; Ritch, 2020; Lyall, 2023;
 High Range driven by Vedder, 2014

Erdafitinib demonstrated efficacy... but also toxicity at a lower dose

THOR-2 TRIAL IR NMIBC

Erdafitinib 6mg (vs. 8 or 9mg in mUC trial)

Design allowed for up to 2 years of Tx

Cohort 3 n=18

CR Rate: _____ 83% (15 of 18)

DOR: _____ 12.7 months (median)

Tx duration: _____ 7.1 months (median)

	ANY GRADE		≥ GRADE 3
Most common AEs	%		%
>1 AE	100		22.2
≥1 TRAE	100		16.7
Hyperphosphatemia	100		
Dry mouth	72.2		
Diarrhea	61.1		5.6
Dysgeusia	50		
Dry skin	38.9		
PPE syndrome	33.3		
Fatigue	33.3		
Abdominal pain	16.7		5.6
Gastritis	5.6		5.6

Source: Daneshmand, 2023 (SUO)

Safety readthrough at lower doses: FGFR-related toxicities were infrequent

	≤60 mg (n=22)		90 mg (n=15)		120 mg (n=4)		All (n=41)	
	Gr. 1-2	≥Gr. 3	Gr. 1-2	≥Gr. 3	Gr. 1-2	≥Gr. 3	Gr. 1-2	≥Gr. 3
ALT increase	1 (5)	—	5 (33)	2 (13)	2 (50)	—	8 (20)	2 (5)
Diarrhea	3 (14)	—	2 (13)	1 (7)	4 (100)	—	9 (22)	1 (2)
Dry mouth	3 (14)	—	6 (40)	—	—	—	9 (22)	—
AST increase	—	—	6 (40)	1 (7)	—	2 (50)	6 (15)	3 (7)
Dry skin	2 (9)	—	2 (13)	—	2 (50)	—	6 (15)	—
Fatigue	2 (9)	—	2 (13)	—	2 (50)	—	6 (15)	—

No hyperphosphatemia at ≤60 mg
No discontinuations or reductions at ≤ 60 mg

TRAEs in >10% of all participants, n (%)

Results are preliminary based on the emerging data from the ongoing Phase 1 portion of the SURF301 study. ALT, alanine aminotransferase; AST aspartate aminotransferase; TRAE, treatment-related adverse event

Our goals for TYRA-300 in mUC, NMIBC and ACH



mUC	Improved tolerability profile for 2L+ mUC in larger Phase 2 study	<i>Further dose optimization</i>
NMIBC	A patient-friendly oral alternative to IVE therapies for NMIBC	<i>Submit Phase 2 IND</i>
ACH	AHV changes leading to differentiated final adult height and functional improvements	<i>Initiate Phase 2 study</i>



Q&A