UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): October 24, 2024

Tyra Biosciences, Inc.
(Exact name of Registrant as Specified in Its Charter)

Delaware	**001-40800**	**83-1476348**
(State or Other Jurisdiction of Incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

2656 State Street **Carlsbad, California**	**92008**
(Address of Principal Executive Offices)	**(Zip Code)**

Registrant's Telephone Number, Including Area Code: (619) 728-4760

(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	**Trading Symbol(s)**	**Name of each exchange on which registered**
Common Stock, par value $0.0001 per share	TYRA	Nasdaq Global Select Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 5.02 Departure of Directors or Certain Officers; Election of Directors; Appointment of Certain Officers; Compensatory Arrangements of Certain Officers.

On October 24, 2024, Siddarth Subramony, Ph.D. resigned from the Board of Directors (the Board) of Tyra Biosciences, Inc. (Tyra or the Company) and the Compensation Committee of the Board (the Compensation Committee) effective immediately. Dr. Subramony's resignation from the Board and the Compensation Committee was not made in connection with a disagreement with the Company on any matter relating to the Company's operations, policies or practices.

Item 7.01. Regulation FD Disclosure.

On October 25, 2024, the Company will host a conference call and webcast to share interim clinical results of TYRA-300 from the SURF301 Phase 1/2 study in metastatic urothelial cancer (mUC). The event will begin at 8:00 a.m. Eastern Time and will be available via a live webcast accessible under the "For Investors" page of Tyra's corporate website, at https://ir.tyra.bio. During the event, the Company will present the corporate slide presentation attached as Exhibit 99.1 to this Current Report on Form 8-K, which is incorporated herein by reference.

The information contained in this Item 7.01, including in Exhibit 99.1 hereto and on Tyra's corporate website, is being "furnished" and shall not be deemed "filed" for the purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the Exchange Act), is not subject to the liabilities of that section and is not deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as shall be expressly set forth by specific reference in such a filing.

Item 8.01 Other Events.

On October 24, 2024, the Company announced interim clinical proof-of-concept data for TYRA-300 in patients with mUC from its ongoing SURF301 Phase 1/2 study.

As of August 15, 2024, the data cutoff date, 41 patients were enrolled in the Phase 1 portion of the SURF301 Phase 1/2 study. Eligible participants were adults with advanced malignancies with or without FGFR3 alterations, including those with prior treatment with erdafitinib. The enrolled patient population was heavily pre-treated, with 44% of patients receiving ≥ 3 lines of therapy prior to receiving TYRA-300, and 76% of FGFR3+ mUC patients receiving ≥ 3 lines of therapy. Treatment with TYRA-300 was evaluated across six dose levels, ranging from 10 mg-120 mg once daily (QD).

- Preliminary PK/PD analysis in 41 patients as of the data cutoff date: TYRA-300 plasma concentrations indicate adequate target coverage at ≥90 mg QD, with further pharmacokinetic characterization ongoing.
- In patients with FGFR3^{+} mUC who received doses ≥ 90 mg QD, anti-tumor activity was observed in all patients:
    - 6 out of 11 (54.5%) patients at ≥ 90 mg QD achieved a confirmed partial response (PR), 3 of which are still ongoing.
    - 5 out of 10 (50%) patients at 90 mg QD achieved a PR.
    - 1 out of 1 (100%) patient at 120 mg QD achieved a PR.
    - A 100% disease control rate (DCR) was achieved for all patients at ≥ 90 mg QD (PR + stable disease).
- TYRA-300 has demonstrated favorable interim safety results as of the data cutoff date:
    - Preliminary data from SURF301 suggest TYRA-300 to be generally well-tolerated, with infrequent FGFR2- and FGFR1-associated toxicities.
    - In doses from 10 mg up to 120 mg QD, there were 4 (10%) serious adverse events related to TYRA-300, 1 dose-limiting toxicity (DLT) of grade (Gr) 3 diarrhea at 90 mg QD, and 1 treatment-related adverse event (TRAE) leading to discontinuation of treatment (Gr3 ALT, 90 mg QD).
    - There were no ≥ Gr4 TRAEs.
    - The 120 mg QD dose was the highest dose evaluated with no DLTs reported.

Forward-Looking Statements

Tyra cautions you that statements contained in this report regarding matters that are not historical facts are forward-looking statements. The forward-looking statements are based on our current beliefs and expectations and include, but are not limited to: the potential safety and therapeutic benefits of TYRA-300. Actual results may differ from those set forth in this report 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; 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 and 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 proposed 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 associated with ODD, including that orphan drug exclusivity may not effectively protect a product from competition and that such exclusivity may not be maintained, or from the RPD Designation, including receipt of a Priority Review Voucher or 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.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	Description
99.1	Slide Presentation
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

TYRA BIOSCIENCES, INC.

Date: October 25, 2024

By: /s/ Ali Fawaz
Ali Fawaz
General Counsel and Secretary

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]	Discovery	IND-Enabling	Phase 1	Phase 2	Phase 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			SURF301			Further QD dose optimization
FGFR2^{ONC}: TYRA-200	~5.5K			SURF201			Complete Ph1
FGFR4/3^{ONC}: TYRA-430	~9K			SURF431			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

SURF301

	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

SURF301

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PK/PD	Dose-dependent activity	Anti-tumor activity observed in all FGFR3+ mUC ≥90 mg QD
SAFETY		

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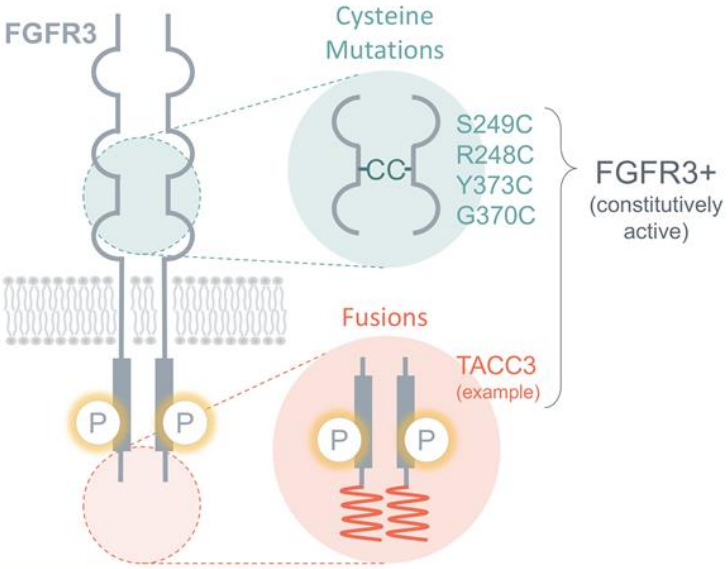
PK/PD	Dose-dependent activity	Anti-tumor activity observed in all FGFR3+ mUC ≥90 mg QD
SAFETY	Safety profile with improved tolerability in FGFR1/2/4-driven toxicities compared to pan-FGFRis	Generally well-tolerated with infrequent FGFR2- and FGFR1-associated toxicities

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.

SURF301 INTERIM PHASE 1 RESULTS

ENA 2024

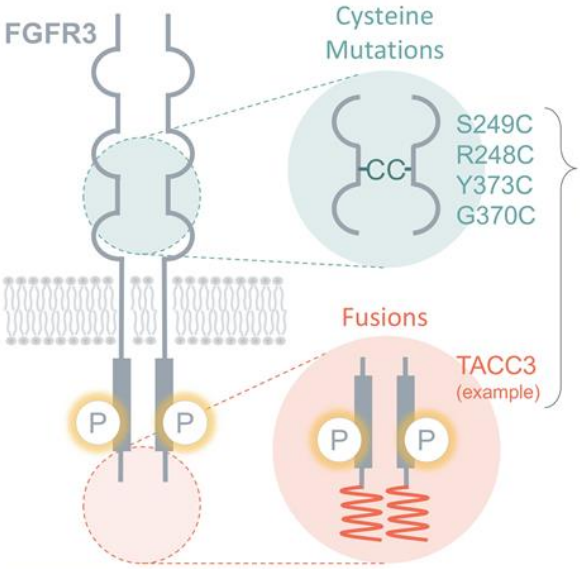
FGFR3 oncogenic alterations are common in bladder cancer



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

FGFR3 oncogenic alterations are common in bladder cancer



	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)

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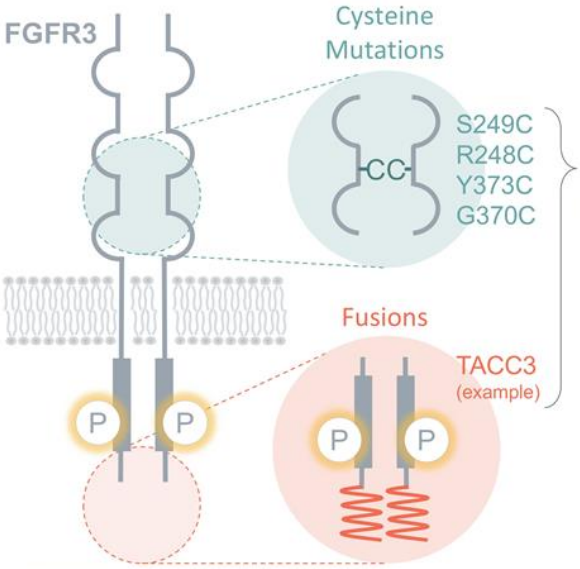

	mUC	NMIBC
FGFR3+	10–20%[1]	40–80%[2]
Oral erdafitinib	35.3% ORR, 12.1mo OS[3] (n=136)	IR: 83% CR[4] (n=18) HR(Cis): 73% CR[5] (n=11)
infigratinib	24% ORR[6] (n=54)	HR (Pap): 75% CR[7] (n=4)
pemigatinib	23% ORR[8] (n=103)	

Abbreviations: IR, Intermediate Risk; HR, High Risk

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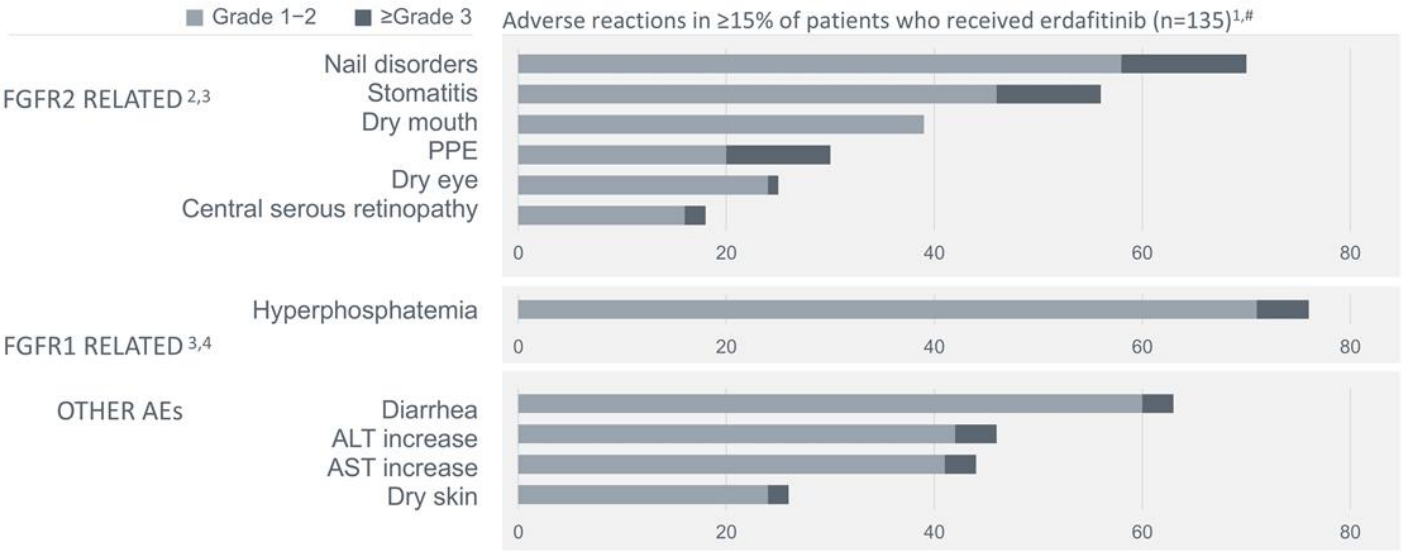
Pan FGFR inhibition is associated with key on-target toxicities



[1]Adapted from: Erdafitinib tablets, for oral use. Prescribing information 01/2024. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/212018s007s008s009lbl.pdf. Accessed 06 October 2024. [2]Lacouture ME et al. Oncologist. 2021. [3]Subbiah V, Verstovsek S. Cell Rep Med. 2023. [4]Kommalapati 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 IC_{50} (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

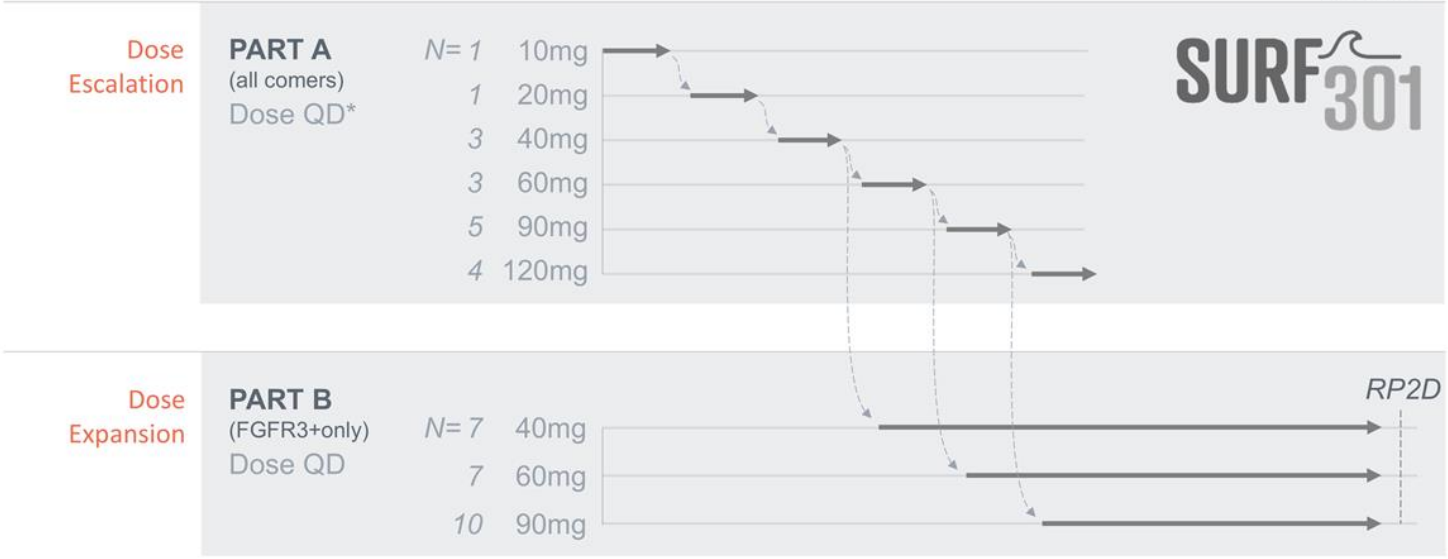
Dose Escalation	**PART A** (all comers) Dose QD*	All solid tumor types[1] FGFR+/-	SURF301
Dose Expansion	**PART B** (FGFR3+ only) Dose QD	Solid tumors with focus on mUC[1] FGFR3+ only	

*1x daily

1. Previously treated patients, including FGFRi, allowed

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

Illustrative



*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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n=41		
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		n (%)
SEX AT BIRTH	Male	30 (73)
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	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)	

1 DLT — 90 mg QD, Gr. 3 diarrhea*

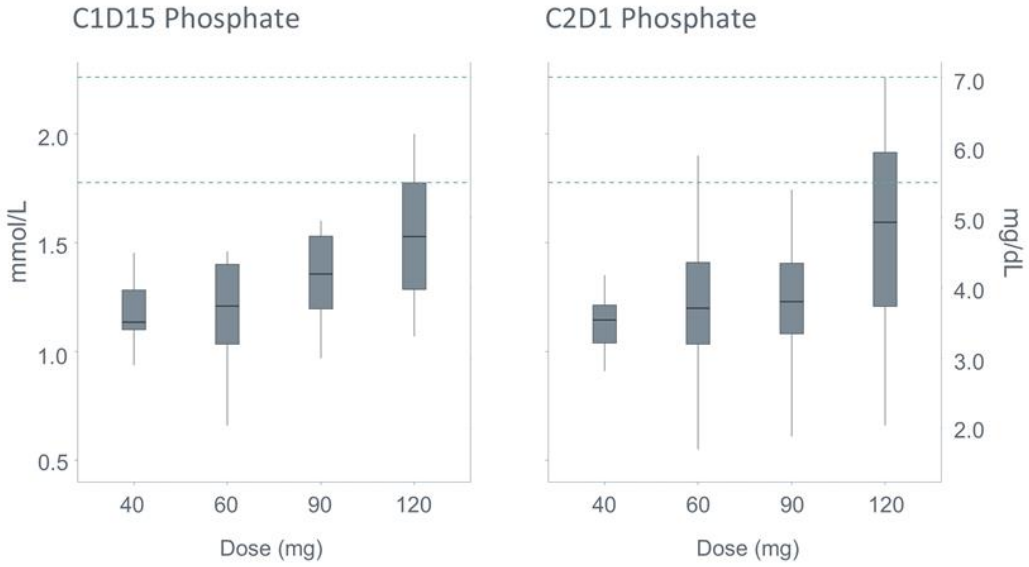
1 Drug-related discontinuation — 90 mg QD, Gr. 3 ALT elevation#

4 Related SAEs — Related to TYRA-300

0 ≥Grade 4 SAE — No drug-related events leading to death

#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

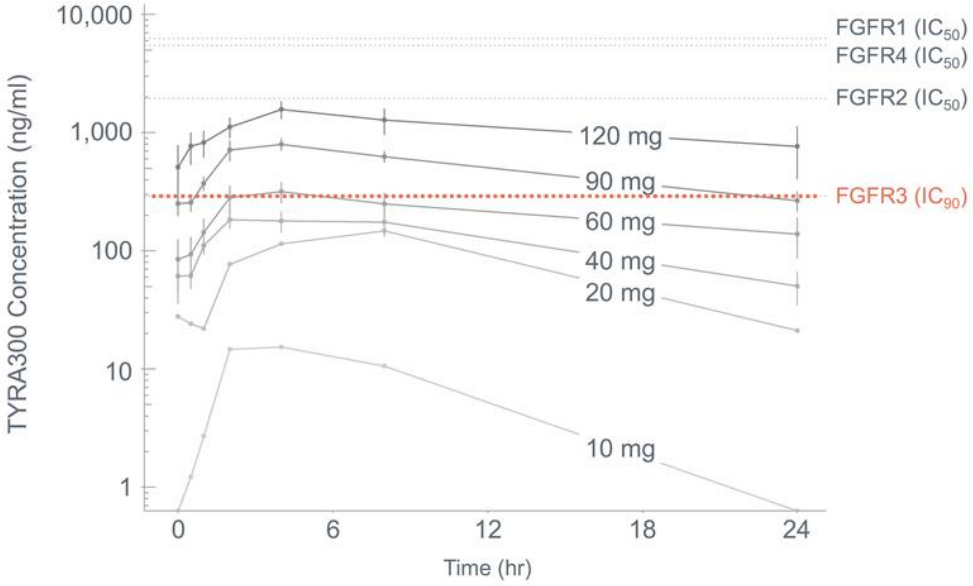
Minimal changes in phosphate at ≤90 mg QD observed



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 Loriot et al. where 5.5- 6.9 mg/dL was defined as Grade 1 and 7.0-8.9 mg/dL as Grade 2.

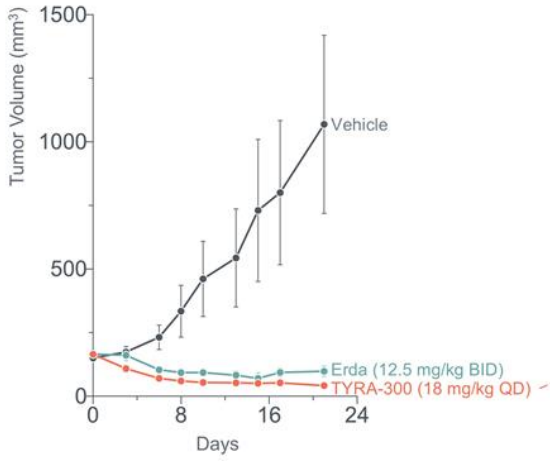
Exposure at doses ≥90 mg exceeded FGFR3 IC_{90} target coverage



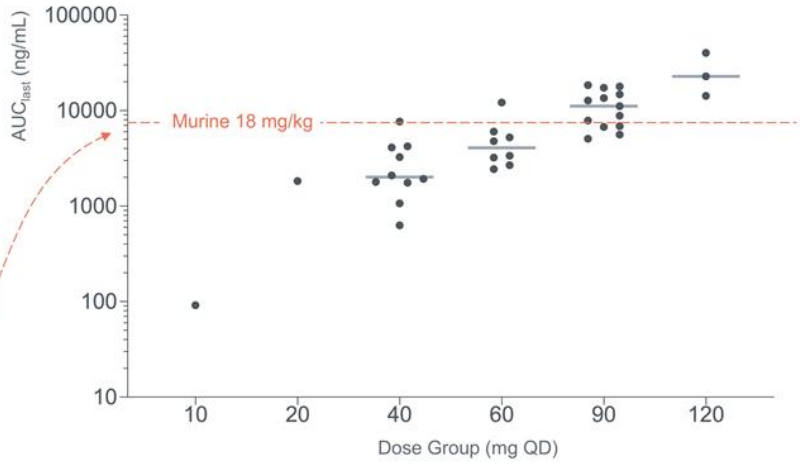
Dose (mg)	N (C1D15)	AUC (ng*h/mL)	
120	3	23,578	2.5x
90	13	10,300	2.4x
60	8	4,360	2.5x
40	10	2,270	
20	1	1,830	
10	1	91.5	

Predicted exposure was achieved in human doses ≥90 mg QD

FGFR3+ UM-UC-14 Xenograft

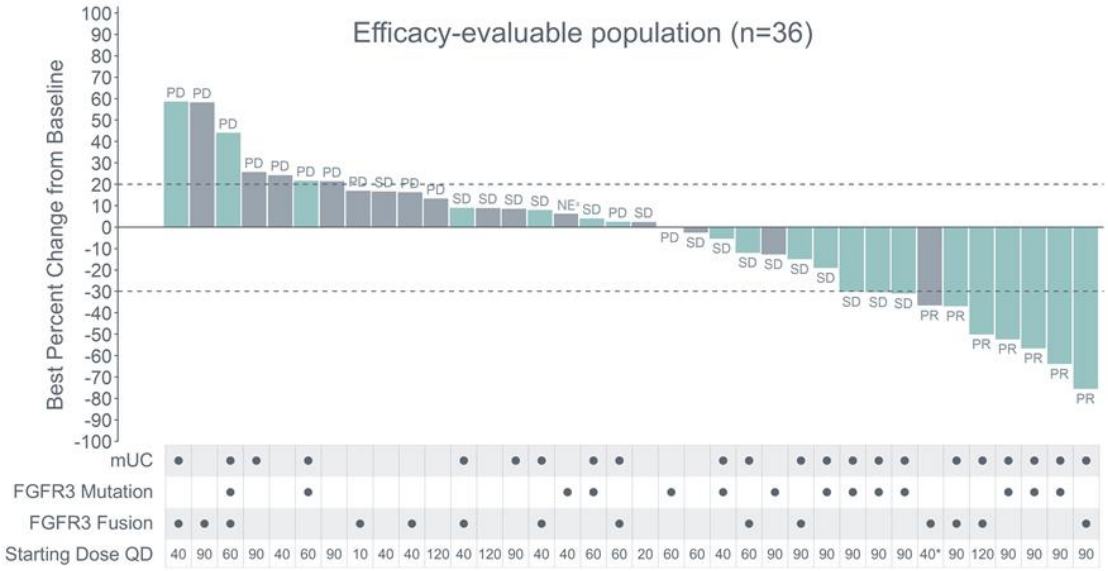


Individual Steady State AUCs in Patients



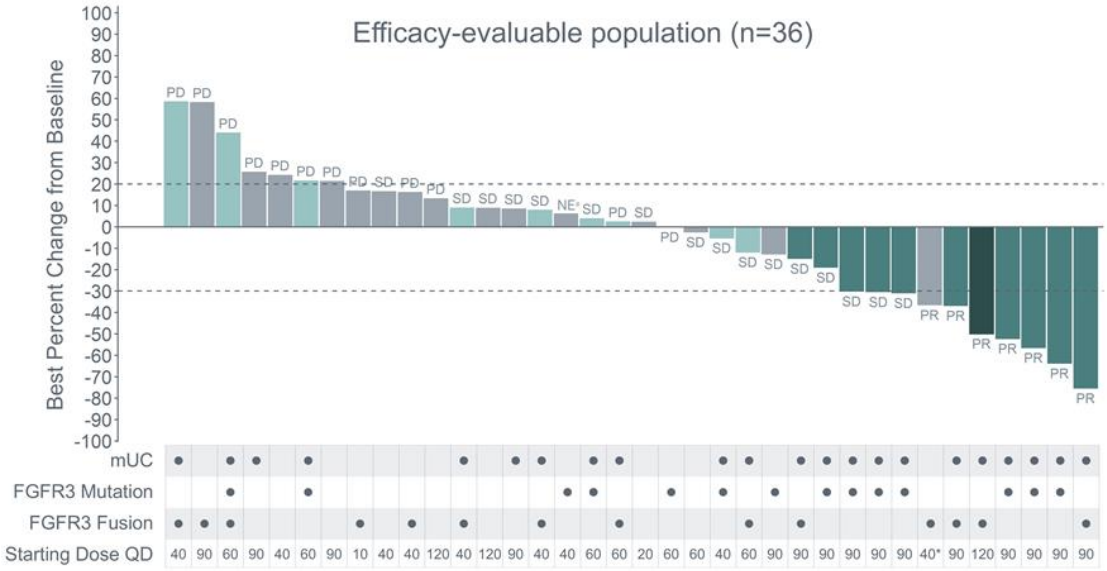
Data on File.

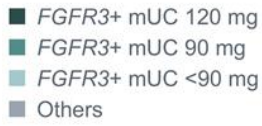
Radiographic tumor response assessment in all evaluable patients



Abbreviations: BOR, best overall response; NE, non-evaluable; PR, partial response; SD, stable disease; PD, progressive disease. N=36/41 evaluable patients. BOR by investigator-assessed by RECIST v1.1. Only confirmed PRs reported. *Participant discontinued due to non-compliance. *Dose-escalation from 40 mg QD to 60 mg QD prior to response

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





Abbreviations: BOR, best overall response; NE, non-evaluable; PR, partial response; SD, stable disease; PD, progressive disease. N=36/41 evaluable patients. BOR by investigator-assessed by RECIST v1.1. Only confirmed PRs reported. *Participant discontinued due to non-compliance. *Dose-escalation from 40 mg QD to 60 mg QD prior to response

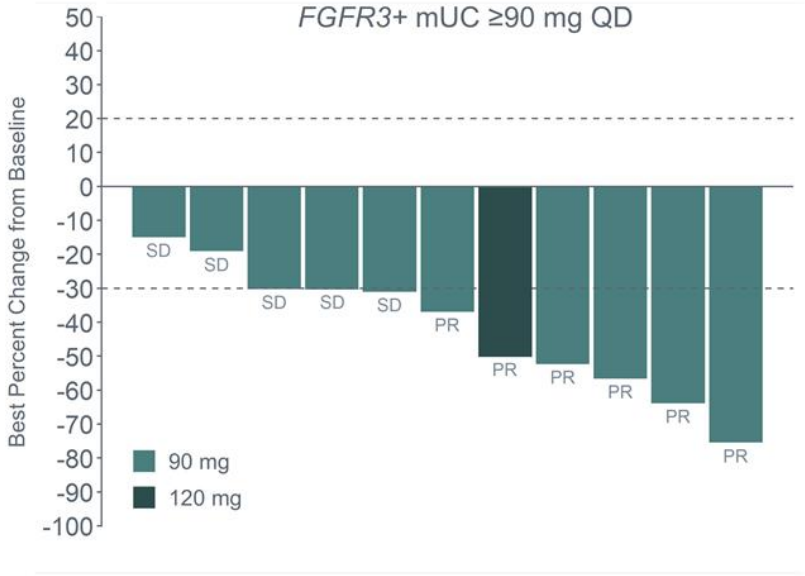
Anti-tumor activity observed in all *FGFR3*+ mUC ≥90 mg QD

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

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

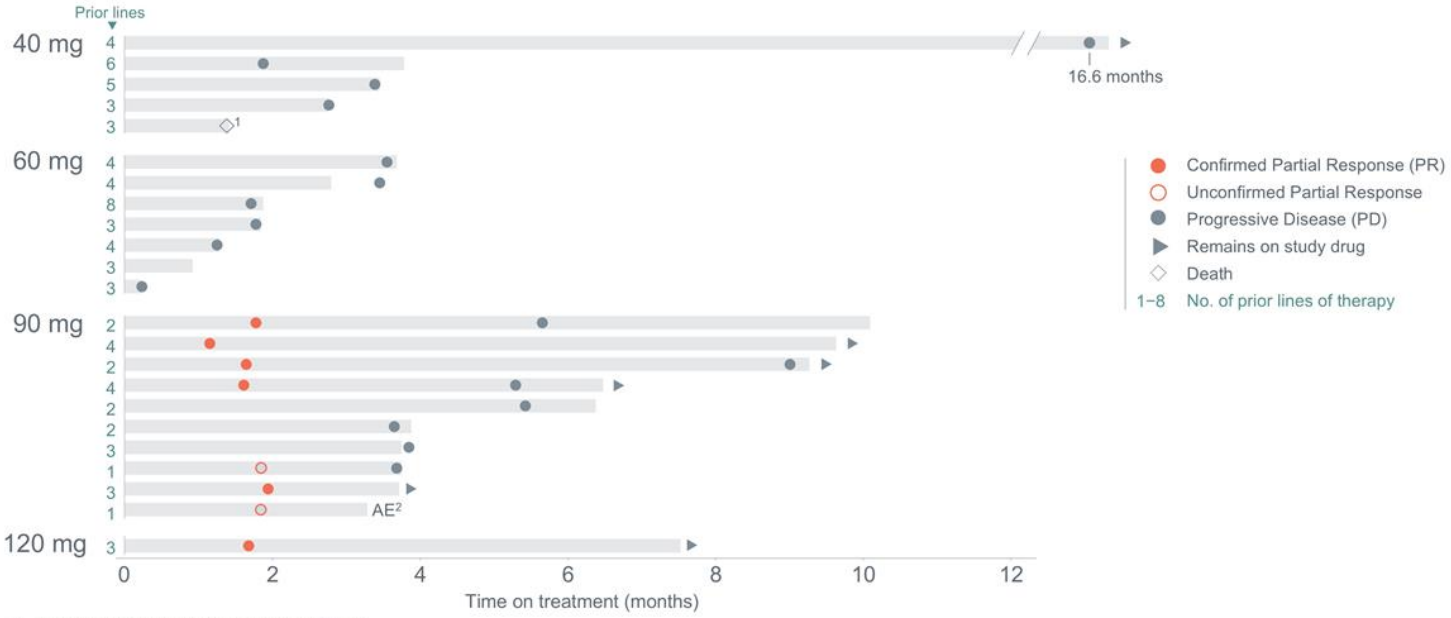
- 5 confirmed PRs at 90 mg QD (n=10)
- 1 confirmed PR at 120 mg QD (n=1)

100% Disease Control Rate



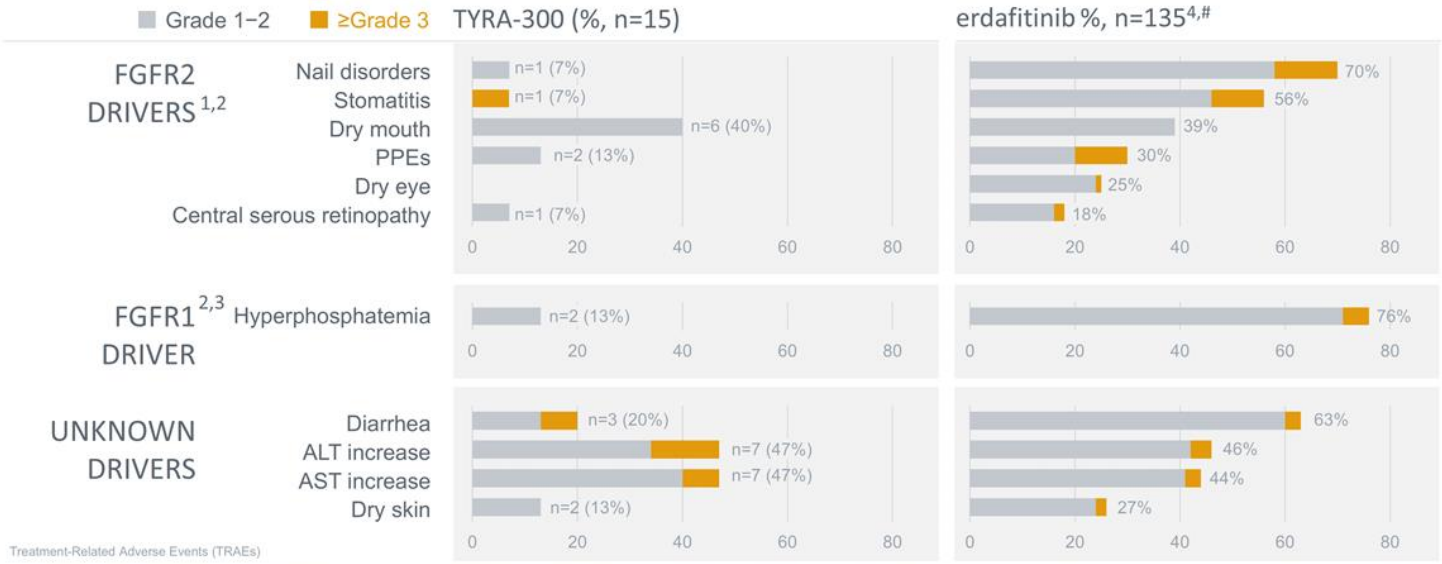
Abbreviations: BOR, best overall response; CR, complete response; PR, partial response; SD, stable disease. Only confirmed PRs reported.
Disease Control Rate: CR+PR+SD

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



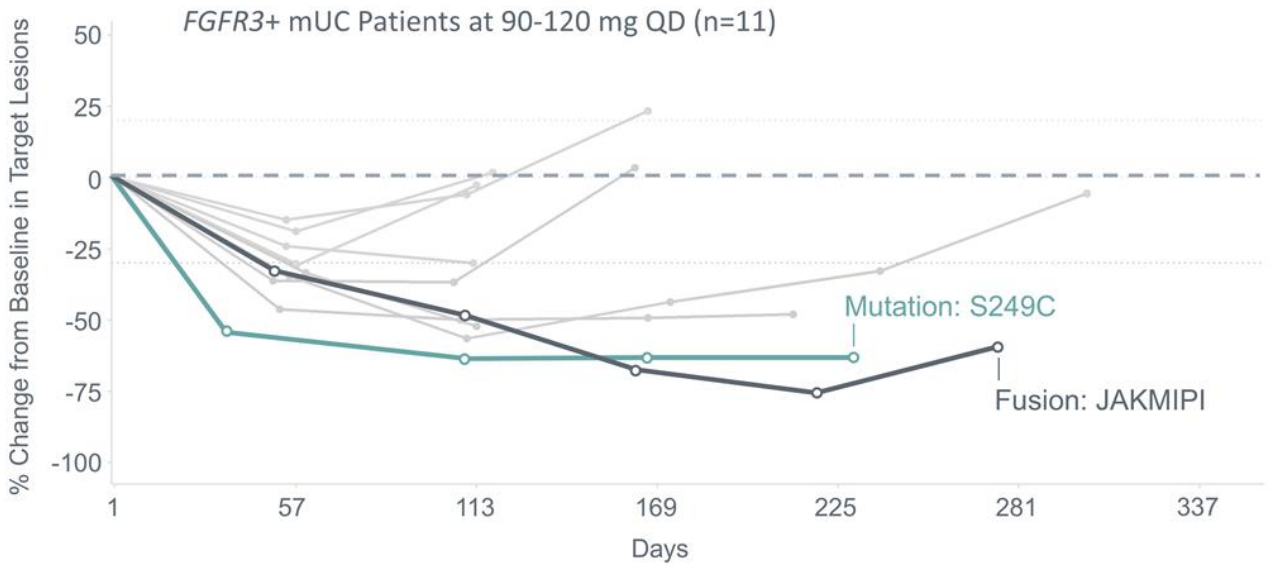
Treatment-Related Adverse Events (TRAEs)

[1]Lacouture ME, et al. Oncologist. 2021. [2]Subbiah V, Verstovsek S. Cell Rep Med. 2023. [3]Kommalapati A, et al. Cancers. 2021. [4]BALVERSA® (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

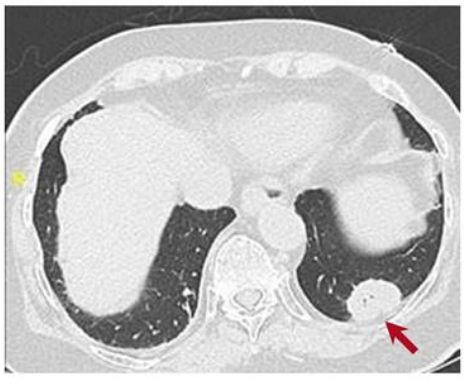
Case study: mUC with activating *FGFR3*^{S249C} mutation

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.*

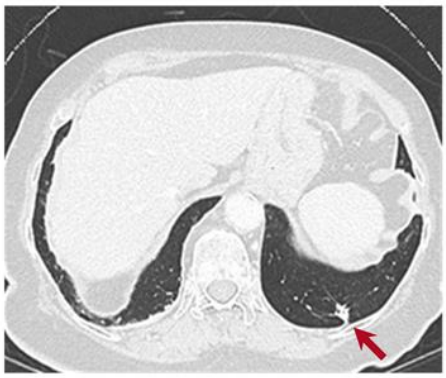
LUNG TARGET LESION

SEPT 25, 2023



Baseline

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

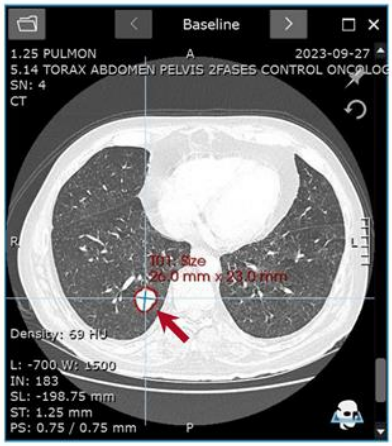
Case study: mUC with activating *FGFR3-JAKMIPI* fusion

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.*

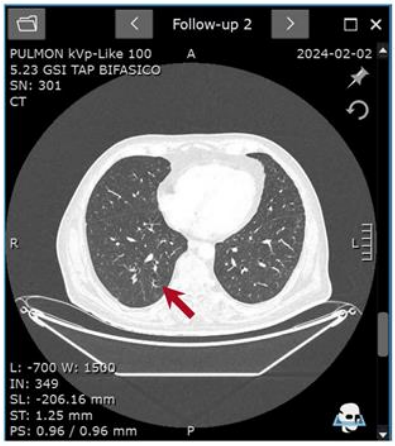
LUNG TARGET LESION

SEPT 27, 2023



Baseline

FEB 2, 2024



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

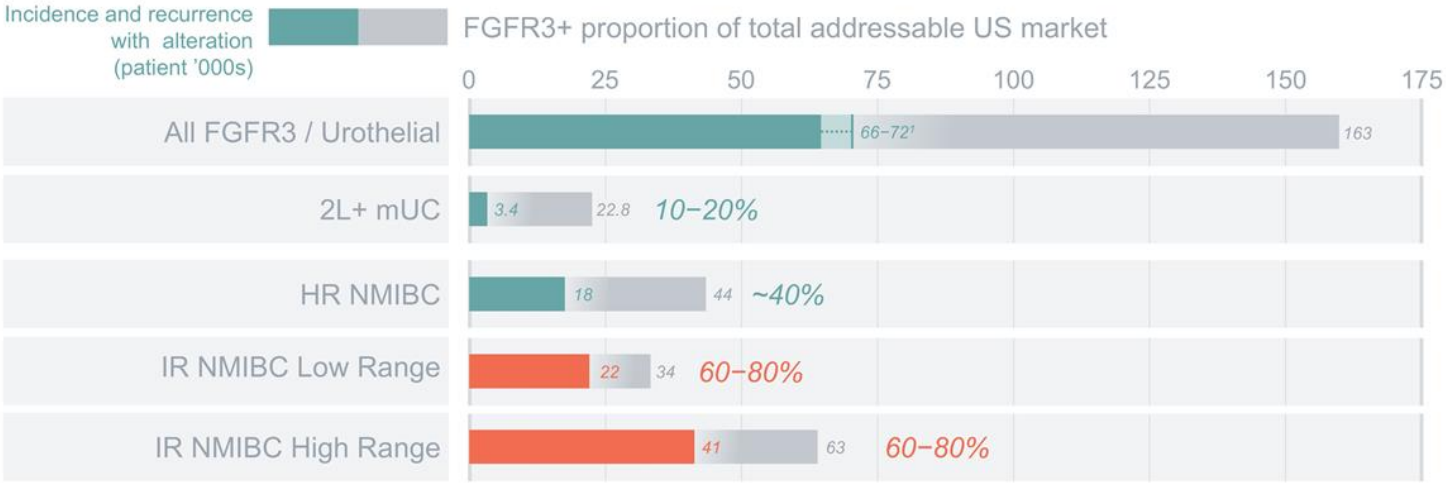
ACH ..... Differentiated efficacy

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.lsapps.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

No hyperphosphatemia at ≤60 mg

No discontinuations or reductions at ≤ 60 mg

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

	≤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)	—

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	*Further dose optimization*
NMIBC	A patient-friendly oral alternative to IVE therapies for NMIBC	*Submit Phase 2 IND*
ACH	AHV changes leading to differentiated final adult height and functional improvements	*Initiate Phase 2 study*

Q&A