Sector: Biotechnology

BUY RECOMMENDATION

Risk Level: High

Market Data	
Share Price	32.47
52-Week High	40.65
52- Week Low	8.98
% of 52 Week High	80%
Market Cap (M)	1,584
Shares Outstanding (M)	59.47
Diluted Market Cap (M)	1,929
Enterprise Value (M)	1,545
Beta	1.43

Financial Metrics	2024	2025	TTM
R&D	80	102	111
% Growth		*29%*	*8%*
Cash & Cash Equivalents	***341.44***	***256.00***	***383.47***
% Growth		*-25%*	*50%*
Total Debt	***6.22***	***5.81***	***5.70***
% Growth		*-7%*	*-2%*
Net Cash	***335.22***	***250.19***	***377.77***
% Growth		*-25%*	*51%*
Key Metrics	**2024**	**2025**	**TTM**
Valuations			
P/B	2.92x	2.06x	5.45x
% Growth		*-29%*	*165%*
EV/R&D	4.64x	14.75x	11.18x
% Growth		*218%*	*-24%*
Liquidity			
Curent Ratio	23.81x	14.67x	20.49x
% Growth		*-38%*	*40%*
Leverage			
Debt to Equity	1.81%	2.24%	1.47%
% Growth		*24%*	*-34%*

Pipeline	Confidence Rating
SURF-302	Low - Moderate
SURF-303	Low - Moderate
BEACH-301	Low

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Tyra Biosciences, Inc. (NASDAQ: TYRA)

"Promising but priced to perfection."

THE BOTTOM LINE

Pareto Capital is establishing a BUY recommendation on Tyra Biosciences, Inc. (NASDAQ: TYRA) with a High Risk rating.

Tyra Biosciences, Inc. (NYSE: TYRA) is a clinical-stage biotech firm focused on developing medicines that target opportunities in fibroblast growth factor receptor (FGFR) biologies. Indeed, Tyra's *Dabogratinib* has high potential, with a large addressable market and a theoretically favourable safety profile due to its targeted mechanism of action. A combination of direct/indirect data has partially validated the efficacy of *Dabogratinib* along with SNAP (their proprietary drug discovery platform). Market sentiment seems to price Tyra as if *Dabogratinib* will indeed produce the intended results throughout subsequent trials. Our analysis harbours contrasting sentiments, with phase 1 data inconclusive due to small sample sizes; the drug's inherent safety remains questionable.

Accordingly, Pareto Capital suggests that although there is potential short-term upside, downside risk may be greater due to pipeline concentration, nuances in study design, and a skewed risk-to-reward ratio. On the other hand, a long-term hold (with the ability to weather potential missed trial endpoints and frequent reassessments) may bring better results. Should the trials produce good data within the next 6 months, and SNAP is accepted into the broader market, future drugs would face higher perceived success rates and market value. This brings us to our thesis. Rather than relying on potential short-term upsides, we believe a longer-term hold on a buy position would both weather the volatility of betting on SURF-302 as a catalyst and reap the benefits of future drugs. Having assessed Tyra's current financial position and evaluated the value in SNAP, we believe the long-term upside is real and palpable.

KEY TAKEAWAYS

- Tyra Biosciences' lead drug candidate Dabogratinib represents a highly valuable long-term asset with a large addressable market across all three diseases (achondroplasia, non-muscle invasive bladder cancer and upper tract urothelial cancer).
- SNAP, Tyra's drug development engine, represents another highly valuable asset if proven, opening the door for additional revenue from drug licensing or future high conviction pipelines.
- Interim data from the SURF-301 trial evaluating Dabogratinib in metastatic urothelial cancer is suggestive but not definitive of high drug specificity and a favourable safety profile. Regardless, there is a foundation supporting the future success of Dabogratinib.
- The recent run-up in share price leaves little room for failure in Tyra's pipelines despite a lack of conclusive data. As a result, the short-term risk-to-reward ratio is skewed due to pipeline concentration and trial design nuance.

BUSINESS OVERVIEW

Tyra Biosciences is a clinical-stage biotechnology company focusing on developing precision medicines targeting fibroblast growth factor receptors (FGFRs) for conditions such as urothelial cancer and achondroplasia (ACH). Its pipeline consists mostly of phase 1 and phase 2 candidates, all designed by its in-house SNAP drug design engine.

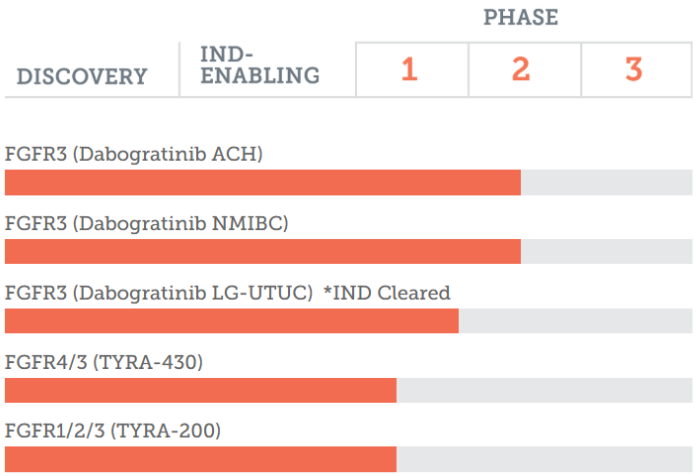


Figure 1. Tyra Bioscience's current clinical pipelines [1]

Their lead candidate, Dabogratinib (formerly TYRA-300), is currently in phase 2 clinical trials as an oral, small-molecule, selective FGFR3 inhibitor for the treatment of ACH, intermediate-risk non-muscle-invasive bladder cancer (IR NMIBC), and low-grade upper tract urothelial cancer (LG UTUC) as part of their 3x3 strategy. The

company has a long cash runway of approximately 32.2 months, supported by recent successful funding rounds, milestones, investments and derisking events.

[1] Tyra Biosciences

LARGE ADDRESSABLE MARKETS IN ACH AND NMIBC

Tyra's most mature candidate is directed towards treating NMIBC and ACH by selectively binding and inhibiting FGFR3, an FGFR isoform responsible for regulating bone growth, cell proliferation, and many other tissue-specific cellular processes. The rationale behind targeting FGFR3 lies within the frequency of ACH and urothelial cancer cases involving an FGFR3 mutation. Approximately 70% of IR NMIBC cases, 90% of all LG UTUC, and 98% of all ACH cases involve a mutation in FGFR3, ultimately leading to tumor formation or stunted bone growth.[2] [3] [4]

ACH is the most common form of dwarfism resulting from insufficient bone growth, affecting 1 in 15,000-40,000 births globally, with a yearly birth prevalence of 4 per 1,000 in North America.[5] [6] Current treatment involves Voxzogo, a daily injectable peptide analog or surgery in life-threatening cases. As shown by Voxzogo's global net sales revenue of $926.9M in 2025, there is high demand for treatment and a large market opportunity for Tyra's Dabogratinib as an oral alternative.[7]

On the side of urothelial cancers, bladder cancer is the fourth most common cancer with 75% of cases being non-muscle invasive, while UTUC only makes up approximately 5-10% of all urothelial cases.[8] [9] Despite differences in their frequencies, both diseases present similar non-invasive treatment opportunities. Standard treatment of IR NMIBC and LG UTUC is often invasive or minimally invasive, either through surgery, chemotherapy, repeated injections/infusions or endoscopy. These are all followed by intensive monitoring due to the high recurrence nature of both diseases. [10] [11]

The increasing need for targeted, non-surgical alternatives has created an opening for Tyra's specific FGFR3 inhibitors.

[2] Klaassen et al., "American Urological Association"
[3] De Lorenzis et al., "Genomic Profiling of Upper Tract," 333.
[4] Pauli, "Achondroplasia," 1.
[5] National Human Genome Research Institute, "About Achondroplasia."
[6] Foreman et al., "Birth Prevalence of Achondroplasia," 2297–316.
[7] Biomarin Pharmaceutical, 2025 Form 10-K
[8] Wen et al., "Low-Grade Non-Muscle-Invasive Bladder Cancer," 846–61.
[9] Kolawa, D'Souza, and Tulpule, "Overview, Diagnosis, and Perioperative Systemic Therapy."
[10] Holzbeierlein et al., "Diagnosis and Treatment of Non-Muscle Invasive Bladder Cancer."
[11] Coleman et al., "Diagnosis and Management of Non-Metastatic Upper Tract Urothelial Carcinoma," 1071–81.

SNAP DRUG DESIGN ENGINE REPRESENTS A PROSPECTIVE VALUABLE ASSET

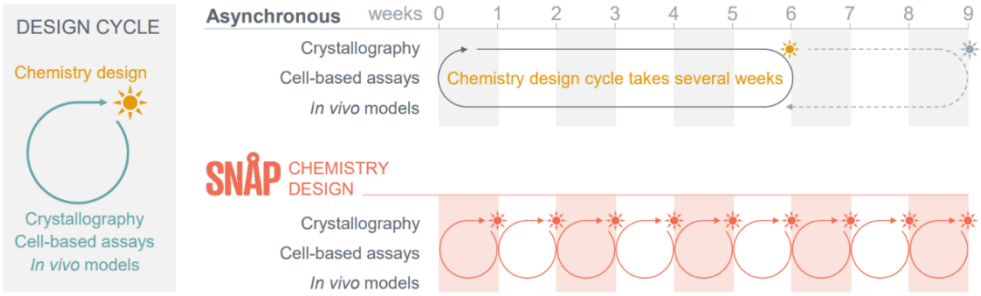


Figure 2. SNAP drug design platform workflow [12]

At the center of Tyra Bioscience's pipeline is their structure-based drug design engine (SBDD), SNAP. Unlike traditional SBDD, SNAP operates on an accelerated cycle, reducing the duration to solve structures from weeks or months to as little as 7 days.[12] This shortened cycle enables rapid refinement and data collection of each structural iteration.

In addition, SNAP also has predictive modelling capabilities which account for potential future gatekeeper mutations, allowing Tyra to develop inhibitors with increased clinical longevity and applicability in oncology. Such capabilities are well-suited towards developing precision medicine, and if proven through positive clinical trial data, would represent a high-value platform capable of generating high conviction pre-clinical drug candidates using gathered empirical data instead of AI-backed simulations or traditional SBDD. Furthermore, validation of SNAP opens the possibility of drug licensing as an additional source of revenue in the future with precision medicine being a rapidly growing field.

DABOGRATINIB (TYRA-300) TYRA'S LEAD ASSET AND PLATFORM VALIDATOR

Dabogratinib is an oral, small-molecule, FGFR3-specific inhibitor designed to achieve effective treatment while limiting side effects associated with inhibiting other FGFR isoforms seen with pan-inhibitors. Classic side effects of FGFR pan-inhibition, such as hyperphosphatemia (high levels of phosphates in the blood), stomatitis (inflammation of the mouth) and gastrointestinal conditions have created a high barrier to entry for oral alternatives as a treatment for difficult-to-access lower-grade cancers such as IR NMIBC and LG UTUC. As a result, the value of Dabogratinib lies in both its convenience as an oral alternative with a favourable safety profile and its role as a SNAP engine validator. Validation is largely dependent on favourable data from Tyra's ongoing phase 2 trials: SURF-301, SURF-302, SURF-303 and BEACH-301.

SURF-301

SURF-301 is an ongoing phase1/2 study evaluating the safety profile and efficacy of Dabogratinib in 22 FGFR3 altered metastatic urothelial cancer (mUC) patients who have undergone prior extensive therapy. Its primary endpoints include determining the maximum tolerated dosage (MTD), recommended phase 2 dose and overall response rate (ORR). Secondary endpoints measure the safety, pharmacokinetics and the long term outcomes of

[12] Tyra Biosciences 2025 Corporate Presentation

patients after drug administration.[13] From released interim data, Dabogratinib was found to have high potency at dose levels above 90mg with respect to the ORR and ctDNA VAF (a molecular indicator of tumor burden).[14]

The SURF-301 study reported an ORR of 54.5%, far above Erdafitinib's phase 3 ORR of 45.6% in the THOR trial (Erdafitinib is the only current FDA-approved oral pan-FGFR inhibitor for mUC).[15] Furthermore, at the molecular level, Dabogratinib achieved a near-complete decrease in ctDNA VAF across most patients, including those with higher baseline ctDNA VAF.[13] Considering the heavily treated patient population in SURF-301, Dabogratinib's demonstrated efficacy in mUC, a highly heterogeneous tumor, highlights promising potential. Additionally, this observed performance in the context of mUC may partially validate SNAP's ability to account for different FGFR3 mutations, with the caveat that it is difficult to pinpoint which specific cells and their associated mutations were targeted. Despite positive indications of efficacy, it is worth noting that both the small sample size (n=22) and the context of a phase 1 trial compared with a phase 3 trial affects the significance of the 54.5% ORR reported relative to Erdafitinib.[13] In reality and subsequent phase 2 and 3 trials, the ORR can be significantly different in either direction and therefore comparisons between the SURF-301 and THOR trials is more relative and directional than definitive.

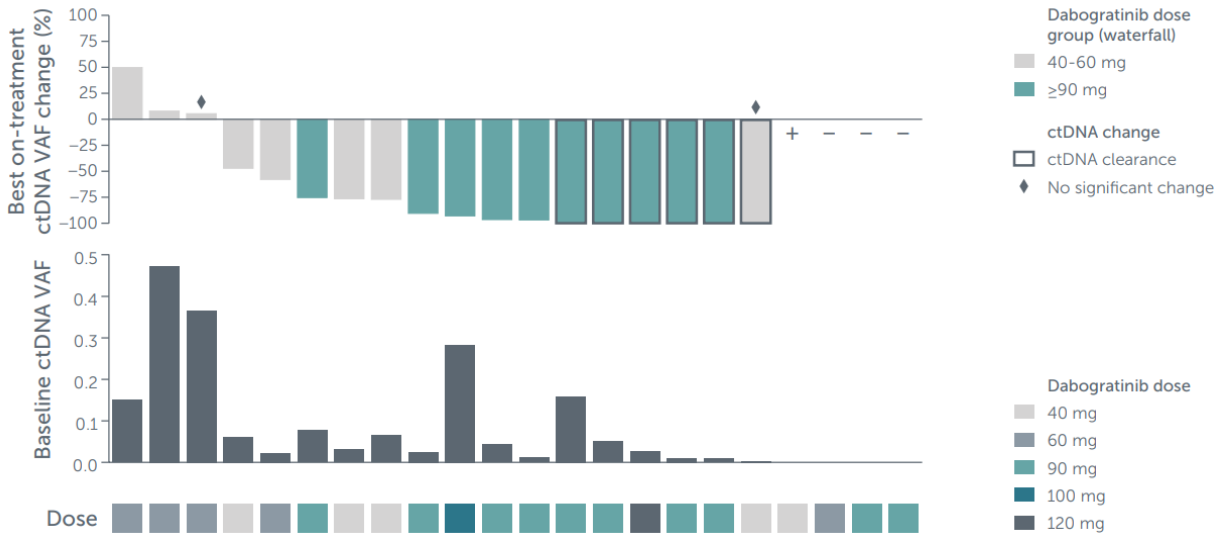


Figure 3. The percentage (%) change in ctDNA VAF in patients administered with 40, 60, 90, 100 and 120mg doses of Dabogratinib. Data was taken from the phase 1 portion of SURF-301.[13]

Regarding SURF-301's Interim safety data, Dabogratinib showed high specificity to FGFR3 compared to other members of the FGFR family. AEs associated with pan-inhibition occurred at low frequencies with no grade 4 or 5 AEs observed across all dosage levels. Most notably, the occurrence of grade 3 AEs was generally low, especially in the ≤60mg treatment group.[13] The absence of hyperphosphatemia, a classic adverse event associated with FGFR1 and FGFR2 inhibition and low frequency of other pan-inhibition associated events (AST increase, ALT increase, dry mouth, and dry skin) in the mentioned ≤60mg treatment group again is indicative of Dabogratinib's selectivity towards FGFR3.[16] Additionally, when compared with Erdafitinib, a superior safety profile is observed with no reported cases of hyperphosphatemia, Palmar-plantar erythrodysesthesia syndrome (PPS), or stomatitis occurring at a frequency above 10% in the Dabogratinib study population (refer to Appendix for Erdafitinib's safety data).

[13] ClinicalTrials.gov, "Safety and Preliminary Anti-Tumor Activity of TYRA-300."
[14] Murtha et al., "ctDNA Monitoring."
[15] Loriot et al., "Erdafitinib or Chemotherapy."
[16] Subbiah and Verstovsek, "Clinical Development," 101204–4.

Despite interim data seeming positive on the surface, the same argument as previous can be made regarding sample size limitations, with the addition of reporting methodology. As only AEs occurring at a frequency >10% in the patient population were reported, individual smaller cases of classic FGFR pan-inhibition-associated AEs may have been omitted. For the reasons stated, safety data from SURF-301 is incomplete and not fully predictive of safety results in subsequent phase 2 trials.

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	4 (18)	—	2 (13)	1 (7)	2 (50)	—	8 (20)	1 (2)
Dry mouth	3 (14)	—	6 (40)	—	—	—	9 (22)	—
AST increase	—	—	6 (40)	1 (7)	1 (25)	—	7 (17)	1 (2)
Dry skin	2 (9)	—	2 (13)	—	2 (50)	—	6 (15)	—
Fatigue	2 (9)	—	2 (13)	—	1 (25)	—	5 (12)	—

Figure 4. The frequency of adverse events (AEs) and their percentage of the total patient population associated with 60, 90 and 120mg doses of Dabogratinib. AEs were only recorded if they occurred in more than 10% of the patient population. AEs observed include: ALT increase, diarrhea, dry mouth, AST increase, dry skin and fatigue. Data was taken from the phase 1 portion of SURF-301.[17]

Considering the mentioned caveats, safety data still indicate strong on-target performance and low inhibition of FGFR1/2/4, while ctDNA VAF assays suggest competitive efficacy. Both factors provide the groundwork to demonstrate the validity of Dabogratinib as an FGFR3-selective small-molecule drug and are positive indicators of the drug's potential success.

SURF-302

SURF-302 is an ongoing phase 2 trial evaluating the safety and efficacy of Dabogratinib in patients with FGFR3 altered low-grade (LG) IR NMIBC. The trial involves 2 confirmed cohorts receiving either a 50mg or 60mg oral dosage daily based on interim results from SURF-301 and a third exploratory cohort. The primary endpoint is the 3-month CR rate, while secondary endpoints include the frequency of AEs and long-term outcomes (progression-free survival, time to recurrence, duration of response & recurrence free survival).[18] SURF-302 is currently Tyra's nearest short-term catalyst, with its primary endpoint data being released before the second half of 2026.

[17] Tyra Biosciences 2025 Corporate Presentation.
[18] ClinicalTrials.gov, "Efficacy and Safety of TYRA-300."

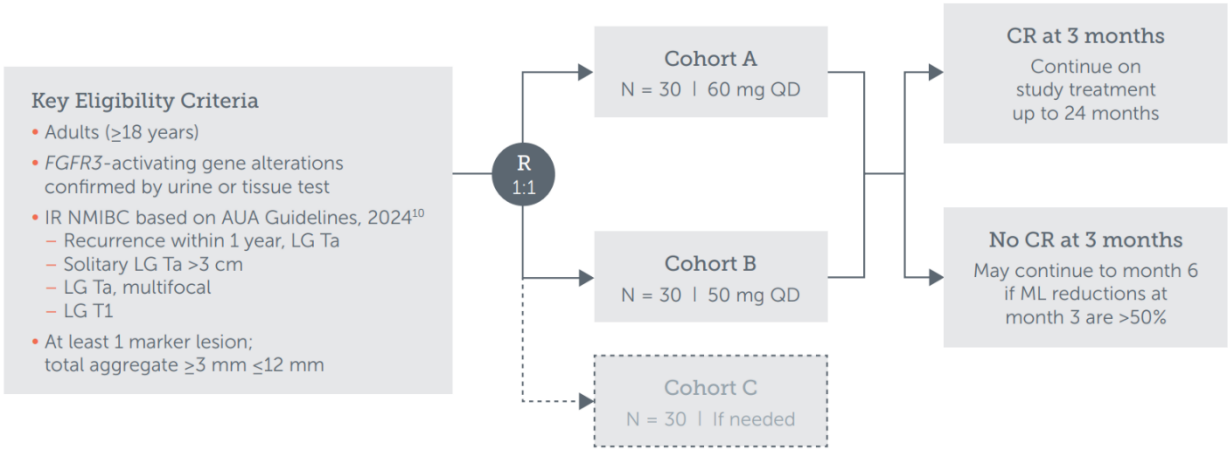


Figure 5. SURF-302 patient inclusion criteria and study design [19]

Based on the 54.5% ORR achieved in phase 1 of SURF-301, SURF-302 may be well-positioned to demonstrate a competitive 3-month CR rate in the FGFR3-altered LG IR NMBC population.[13] Given that the patient population of SURF301 has mUTC, a categorically more heterogeneous and resistant tumor than LG IR NMIBC for FGFR3, some data can be cautiously extrapolated between the two diseases to inform reasonable expectations (see Appendix for supporting evidence from the SURF-301 ctDNA VAF assay). On the molecular level, Dabogratinib has shown positive anti-tumor activity across mUC patients of differing tumor burden. Although mUC and IR NMIBC are different diseases, IR NMIBC is categorically less heterogeneous and commonly features a higher FGFR3 mutation rate relative to other FGFR isoforms. As a result, the demonstrated molecular activity supports the plausibility of a competitive CR rate within the context of SURF-302. On a comparative basis, Erdafitinib has shown a 3-month CR rate of 89% in a similar cohort to that recruited in SURF-302. This cohort was part of the phase 2 THOR-2 trial, evaluating the efficacy and safety profiles of Erdafitinib in patients with FGFR3-altered IR NMIBC.[20] Despite Erdafitinib's role as a pan-inhibitor, selection within THOR-2 for FGFR3 altered patients minimizes the probability of responses resulting from FGFR pan-inhibition. As a result, comparable CR rates between the two drugs is plausible.

Tyra has cited 70% as their competitive 3-month CR endpoint expectation.[17] This is consistent with the recently FDA-approved Zusduri (UGN-102) for LG IR NMIBC, which demonstrated an 80% CR rate in its phase 3 study while being a minimally invasive treatment.[21] Although the same sample size limitations of SURF301 (n=22) should be considered, results from the ctDNA VAF assay and Erdafitinib's CR rate in IR NMBC do indicate a positive outlook for Dabogratinib in IR NMIBC. As a result, a CR rate of approximately 70% is moderately likely and may be competitive for phase 3 FDA approval, provided the safety profile of Dabogratinib allows higher dose levels and, therefore, greater FGFR3 inhibition. For the remaining secondary endpoints, there is currently insufficient data to reliably predict the progression-free survival (PFS) and recurrence-free survival (RFS) for Dabogratinib in LG IR NMIBC. These endpoints are to be determined by the trial itself.

Sample size limitations and the reporting methodology used by Tyra in their SURF301 trial leave little room for confidence regarding Dabogratinib's safety profile. Regardless, a low occurrence of grade 3 AEs and major pan-inhibition-associated events in the 50mg and 60mg groups is possible and already partially supported by SURF-301 interim data. Being a non-invasive treatment, Dabogratinib's safety profile is arguably the most important factor in

[19] Jayram et al., "Evaluating the Efficacy and Safety of Dabogratinib."
[20] Daneshmand et al., "Erdafitinib in Patients,"
[21] Prasad et al., "UGN-102."

its commercial and clinical trial success. Current treatment and the severity of LG IR NMIBC has acted as a barrier of entry for pan-inhibitors like Erdafitinib where the effects of adverse events outweigh efficacy. As such, the safety profile of Dabogratinib is greatly interconnected with its efficacy, where both a clean safety profile and high efficacy is required to justify usage. With incomplete SURF-301 safety data, at most only moderate confidence can be assigned to Dabogratinib for the treatment of LG IR NMIBC as safety outweighs efficacy in this specific scenario.

Considering Dabogratinib's molecular activity in SURF-301, Erdafitinib's competitive CR rate as a pan-inhibitor of FGFRs in an FGFR3 altered population and the low heterogeneity nature of LG IR NMIBC, only low to moderate confidence can be assigned to Dabogratinib for the treatment of LG IR NMIBC. Although SURF-301 serves as a positive indicator for both safety and efficacy, due to incomplete data and a small sample size (n=22), high confidence in the trial's success cannot be justified.

SURF-303

SURF-303 is an ongoing phase 2 trial in recruitment evaluating the efficacy and safety of Dabogratinib in LG UTUC patients. Unlike SURF-302, participants are not selected for FGFR3 alterations or fusions, making the population more diverse. The study features 2 confirmed cohorts: i) 80mg dosage group, ii) 60mg dosage group, and a third exploratory cohort. Both the primary and secondary endpoints are identical to those in SURF-302.[22]

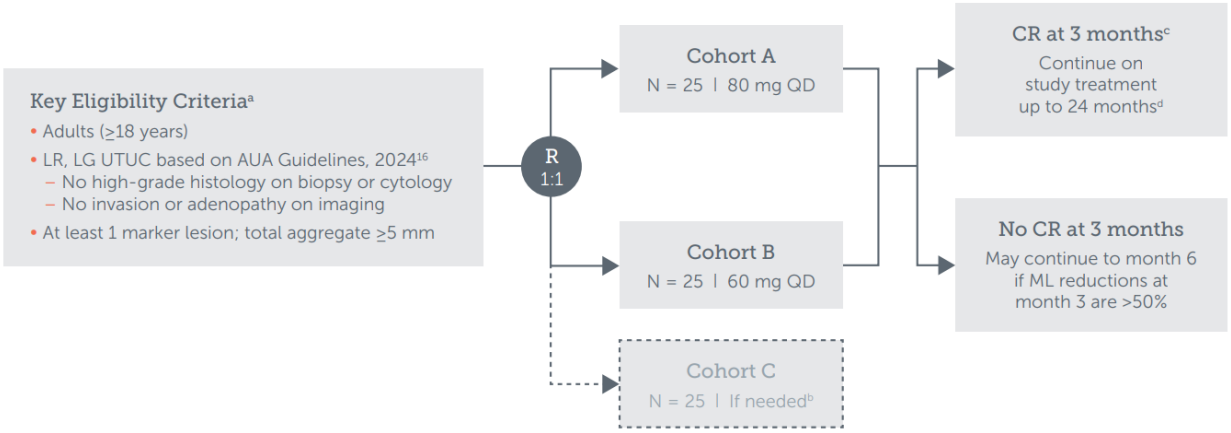


Figure 6. SURF-303 patient inclusion criteria and study design [23]

The same expectations on the 3-month CR rate cannot be carried over from SURF-302 to SURF-303 due to the biomarker-unselected patient population. Although LG UTUC is associated with a high prevalence of FGFR alterations, the lack of a pre-screen for FGFR-altered patients poses the risk of CR rate dilution. As such, SURF-303's study design is a double-edged sword where a competitive CR rate despite a non-biomarker selected population can easily lead to phase 3 FDA approval at the risk of possible endpoint dilution. Furthermore, there have been limited studies on the efficacy of FGFR inhibition for localized UTUC, with the only notable study being a phase 1b trial using Infigratinib. Although a 66.7% ORR with significant tumor size shrinkage was achieved in the mentioned study, sample size limitations remain, early termination undermined results and the differences between pan-inhibition and specific inhibition cannot be ignored.[24] Therefore, due to the lack of comparable data and the risk

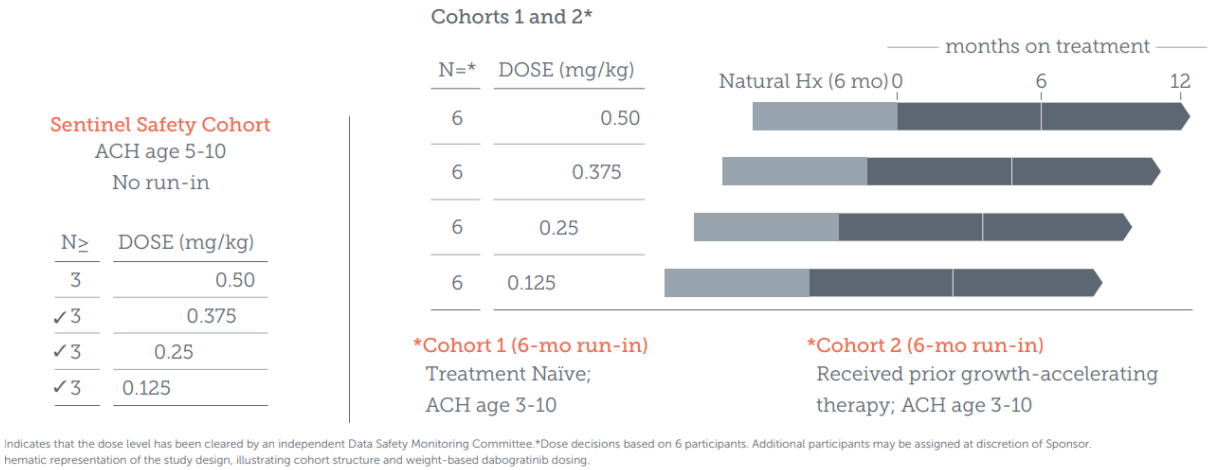
[22] ClinicalTrials.gov, "Phase 2A/B Efficacy and Safety of Dabogratinib."
[23] Matin et al., "Evaluating the Efficacy and Safety."
[24] Matin et al., "Evaluating Tolerability and Activity," 784–93.

of CR rate dilution, results from SURF-303 remain highly uncertain and depend on the proportion of patients with an FGFR3 alteration. However, a 66.7% ORR does suggest the validity of FGFR3 inhibition in treating LG UTUC.

In terms of safety profile, expectations from SURF-302 can be carried over due to similar patient inclusion criteria, with the exception of biomarker selection. As SURF-302 is set to complete before SURF-303, safety data from the LG IR NMIBC population can be utilized in the future to readjust expectations. As an approximate benchmark, Dabogratinib likely needs a 50%+ CR rate in this phase with a favourable safety profile to qualify for phase 3. The 50%+ CR rate threshold is derived from the current treatment of LG UTUC, Jelmyto on the basis that UGN-104, a reformulation of Jelmyto, recently received FDA approval for a phase 3 trial using Jelmyto's 59% CR rate in the OLYMPUS trial.[25] [26] Although phase 3 studies often yield lower CR rates, the OLYMPUS trial's 59% CR represents the most clinically relevant data available. In order to progress to phase 3, Dabogratinib must set a comparable CR rate and have a favourable safety profile in phase 2 to justify the need for an oral alternative. For the same reasons stated above and in SURF-302, only low to moderate confidence is assigned to the success of SURF-303.

BEACH-301

BEACH-301 is Tyra's ongoing phase 2 trial designed to target other diseases outside of cancer. The study focuses on the efficacy and safety of Dabogratinib in children aged 3-10 with ACH associated with the G380R mutation in FGFR3. The study splits participants into 3 cohorts: i) sentinel, ii) Children who have received no prior growth-accelerating treatment, and iii) Children who have received prior growth-accelerating therapy. The latter two cohorts' dosage levels will be determined based on safety data from the sentinel group. Primary end points include the frequency of AEs and the change in annualized growth velocity (AGV) while secondary endpoints include standardized change in height, anthropometric measurements (height, weight, BMI, body ratios…) and Dabogratinib's pharmacokinetic properties.[27]



Indicates that the dose level has been cleared by an independent Data Safety Monitoring Committee.*Dose decisions based on 6 participants. Additional participants may be assigned at discretion of Sponsor.
hematic representation of the study design, illustrating cohort structure and weight-based dabogratinib dosing.

Figure 7. BEACH-301 study design [28]

Although it has been partially proven that Dabogratinib is effective and selective for FGFR3, its effects on AGV is still uncertain due to a lack of direct preliminary data. However, comparisons can be made with the recent PROPEL 2 and PROPEL 3 studies, which evaluated the safety and efficacy of Infigratinib in children aged 3-11 with ACH.

[25] ClinicalTrials.gov, "Study of UGN-104."
[26] Kleinmann et al., "Primary Chemoablation," 776–85.
[27] ClinicalTrials.gov, "Study of TYRA-300 in Children."
[28] Tyra Biosciences, "BEACH-301."

Throughout the duration of PROPEL 2, Infigratinib achieved an AGV difference to the placebo group of +3.36 cm/year at the 6-month mark and +2.51cm/ year at the 18-month mark.[29] Similar results were seen in PROPEL 3 where a +2.10cm/ year AVG difference was achieved between the treatment and placebo groups at the 52 week mark.[30] With Dabogratinib's FGFR3 selectivity and the majority of ACH involving an FGFR3 alteration, comparable AVG differences can be achieved with a similar or more competitive safety profile than Infigratinib. If Dabogratinib demonstrates a superior safety profile and a clear dose-efficacy relationship, higher doses of Dabogratinib can be administered to achieve a greater AVG difference than Infigratinib. This potential dose-dependent relationship is also well supported within PROPEL 2, where higher dosage levels translated to higher AVG differences.[27] To qualify for phase 3, Dabogratinib likely will not need an AVG change equal to that of Infigratinib. Instead, the benchmark is likely Voxogo's +1.57 cm/ year AVG change for a high chance of approval in addition to a clean safety profile. However, for successful commercialization, the bar sits above Infigratinib's 2.10 cm/year AVG change as Infigratinib has shown minimal adverse events at tested doses. Unless Dabogratinib is able to be administered at a higher dosage while maintaining a clean safety profile to achieve an AGV change > 2.10 cm/year, breaking into the ACH market within the future remains a challenge given that Infigratinib is in the process of submitting an NDA (New Drug Application) and will likely be approved.

As of present, Tyra has announced completion of all dosage levels (0.125, 0.25, 0.375 and 0.5mg/kg) in the sentinel group with no adverse events.[31] Based on SURF-301 and pre-clinical data comparing Dabogratinib's selectivity for FGFR3 in comparison to other pan-inhibitors, we can predict that the same dosage-efficacy relationship demonstrated in PROPEL 2 holds. Although this dosage relationship is to be expected, it is still unclear whether 0.5mg/ kg of Dabogratinib is enough to stimulate adequate growth. As Dabogratinib is the first FGFR3 specific inhibitor, there are no similar comparisons to relate dosage levels to specific AGV changes to make meaningful predictions.

Overall, based on current benchmarks, pre-clinical data and sentinel cohort data, low confidence is assigned to both the efficacy and safety profile of Dabogratinib in ACH. 2.10 cm/ year AGV serves as a benchmark that is achievable due to the broader mechanistic similarities between Infigratinib and Dabogratinib and ACH's FGFR3 alteration bias. However, unlike SURF-302 and SURF-303, there is limited evidence from a direct supporting study to confirm the efficacy of Dabogratinib in ACH.

Near-term Data Readouts

Tyra has announced 3 key data readouts for 2026: i) 3-month CR rate for SURF-302 before the start of 2H 2026, ii) Initiation of SURF-303 within 2026, iii) Safety data for the remaining sentinel cohort dosage groups within 2H 2026 of BEACH-301.

RISKS & MITIGATIONS

Currently, Tyra Biosciences stands at a rare intersection within the biotech industry. While significant derisking events have occurred, including funding and positive data readouts, many concerns remain for the company, both in the short and long term.

[29] Savarirayan et al., "Oral Infigratinib Treatment."
[30] BridgeBio Pharma Inc, "Positive Phase 3 Topline Results."
[31] Tyra Biosciences Q1 2026 Financial Results.

The most significant risk Tyra faces is **regulatory risks** from the FDA. This is especially true with ACH where the treatment population are children aged 3-10. Dabogratinib must produce a highly favourable safety profile and will be under high scrutiny from the FDA in both their results and trial design. Furthermore, the lack of an established oral alternative in IR NMIBC and LG UTUC makes Dabogratinib the benchmark for FDA approval. Although this is a good barrier to entry once Dabogratinib is commercialized, it leads to a high level of uncertainty around the efficacy and safety profile required for an NDA.

Another common concern with biotech companies is the **risk of dilution.** Despite Tyra's recent success in raising capital, leading to 32.2 months of cash runway, the transition of Dabogatinib's trials into phase 3 will significantly increase their burn rate. Considering the progress of SURF-302 and SURF-303, simultaneously running two phase 3 trials, which typically take around 12 months, puts a heavy cash burden on Tyra, increasing the risk of stock dilution. As all of Tyra's pipelines progress, further dilution becomes more likely due to the pre-commercial nature of Tyra.

On the structural level, Tyra's 3x3 strategy with Dabogratinib poses a **single asset dependency risk**. Although there are phase 1 trials targeting multiple FGFRs with a different molecule, Tyra's pipeline remains heavily concentrated on the performance of Dabogratinib. While their phase 1 trials mature, Dabogratinib takes the spotlight as the key driver of Tyra's near-term performance, with both SURF-303 and BEACH-301's success being linked to the upcoming 3-month CR rate readout of SURF-302. With FGFR3 being the key target for all 3 diseases, any data indicating Dabogratinib's poor efficacy in one disease raises concerns around the SNAP platform and success in other targeted diseases. While poor data in one trial will not scientifically invalidate the others due to mechanistic differences between the diseases, the more immediate consequence would be stock price compression and increased difficulty in raising capital for phase 3.

In terms of specific pipelines, Tyra's moat in non-invasive alternatives makes them a first mover in orally administered FGFR3 inhibitors in IR NMIBC and LG UTUC. However, within the ACH market, Tyra faces a potential **second-mover disadvantage** with the planned NDA submission for Infigratinib. Dabogratinib's late entry into the market increases the need for it to differentiate itself in both safety profile and AGV. In addition to the raised performance baseline, commercialization as a second-mover is often slow due to a lack of real-world treatment data and the existence of an established treatment within the same niche.

APPENDIX

Erdafitinib Safety Data

Event	Erdafitinib (N=135)			
	Any Grade	Grade 1	Grade 2	Grade ≥3
	number (percent)			
Hyperphosphatemia	108 (80.0)	70 (51.9)	31 (23.0)	7 (5.2)
Stomatitis	65 (48.1)	22 (16.3)	32 (23.7)	11 (8.1)
Dry mouth	53 (39.3)	45 (33.3)	8 (5.9)	0
Palmar–plantar erythrodysesthesia syndrome	41 (30.4)	6 (4.4)	22 (16.3)	13 (9.6)
Alanine aminotransferase increased	37 (27.4)	24 (17.8)	9 (6.7)	4 (3.0)
Alopecia	34 (25.2)	29 (21.5)	4 (3.0)	1 (0.7)
Dry skin	31 (23.0)	23 (17.0)	6 (4.4)	2 (1.5)

Aspartate aminotransferase increased	29 (21.5)	21 (15.6)	5 (3.7)	3 (2.2)
Fatigue	20 (14.8)	12 (8.9)	8 (5.9)	0

Table 1. Frequency of AEs and their percentage of the total patient population from the phase 3 THOR trial of Erdafitinib. Patients were given 8-9mg of Erdafitinib daily. [12]

Dabogratinib Specificity Data

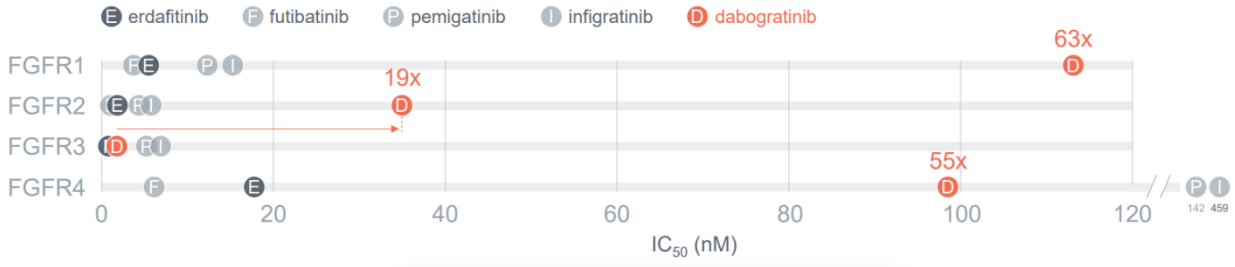


Figure 8. Dabogratinib's IC50 (Half maximal inhibitory concentration) in comparison to Erdafitinib, Futibatinib, Pemigatinib and Infigratinib [11]

SRUF-301 ctDNA VAF Assay Data

1. mUTC patients with lower baseline ctDNA VAF who were administered between 40mg and 60mg of Dabogratinib showed a 50-70% decrease in ctDNA VAF, suggesting positive anti-tumor activity in FGFR3-altered patients.
2. A dosage of ≥90mg has shown significant responses (from ~75-90% decreases in ctDNA VAF) across all patients regardless of baseline ctDNA VAF levels, again demonstrating positive anti-tumor activity.[13]

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