Tyra Biosciences Reports Interim Clinical Proof-of-Concept Data for TYRA-300, an Investigational Oral FGFR3-Selective Inhibitor, in Phase 1/2 SURF301 Study in Patients with Metastatic Urothelial Cancer (mUC)

- Encouraging preliminary anti-tumor activity observed in heavily pre-treated population -

- At ≥ 90 mg QD, 6 out of 11 (54.5%) patients with FGFR3+ mUC achieved a confirmed partial response (PR), with 100% disease control rate and sustained duration of activity -

- Positive safety results across all QD doses,with infrequent FGFR2/FGFR1-associated toxicities -

- Conference call scheduled for October 25th, 2024, at 8AM EDT -

CARLSBAD, Calif., Oct. 24, 2024 /PRNewswire/ -- Tyra Biosciences, Inc. (Nasdaq: TYRA), a clinical-stage biotechnology company focused on developing next-generation precision medicines that target large opportunities in Fibroblast Growth Factor Receptor (FGFR) biology, announced today clinical proof-of-concept data for TYRA-300 in patients with metastatic urothelial (mUC) cancer from its ongoing SURF301 Phase 1/2 study. These data will be presented in a late-breaking oral presentation at the 36th EORTC-NCI-AACR (ENA) Symposium on Molecular Targets and Cancer Therapeutics, being heldOctober 23-25, 2024 in Barcelona, Spain. TYRA-300 is a potential first-in-class, investigational, oral, FGFR3-selective inhibitor designed to avoid the toxicities associated with inhibition of FGFR1, FGFR2 and FGFR4, while being agnostic for the FGFR3 gatekeeper mutations.

"FGFR3 alterations are known to drive tumor biology in a subset of urothelial cancer. While pan-FGFR inhibitors have demonstrated benefit and are approved for use in FGFR3 altered urothelial cancer, they are associated with multiple intolerable on-target toxicities that limit their clinical utility. There remains an unmet need to deliver improved precision medicine for urothelial cancer patients, that allow patients to not only live longer, but live better," said Ben Tran, M.D., Associate Professor, Peter McCallum Cancer Centre, Melbourne, Australia. "The initial results from TYRA-300 are very encouraging. I believe TYRA-300 has the potential to be a next generation targeted therapy, with high selectivity for FGFR3. These early data provide support that TYRA-300 can deliver improved anti-tumor activity and tolerability for our FGFR3 altered urothelial cancer patients. TYRA-300 has real potential to improve outcomes, and I look forward to its continued development in all FGFR3 altered cancers."

Summary of Interim Clinical Results

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 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.

"The preliminary data are what we were expecting to see with TYRA-300, being generally well-tolerated with fewer toxicities, and anti-tumor activity in FGRF3+ mUC patients," said Doug Warner, M.D., Chief Medical Officer of TYRA. "The emerging profile of TYRA-300 supports further development in metastatic urothelial cancer, where an attractive opportunity exists for a more tolerable option in second line."

Dr. Warner continued, "We are grateful for the support of our study participants, their families and our global collaborators on SURF301. We remain focused on progressing TYRA-300 through dose optimization in SURF301 and toward patients in need."

"Our team set out to solve an ambitious chemistry problem that had stumped the field of precision oncology - to create an efficacious FGFR3-selective inhibitor with a favorable tolerability profile to address the limitations of pan-FGFR inhibitors. We believe that today's interim results provide clinical support for addressing this difficult problem, and the data are in line with our expectations," said Todd Harris, CEO of TYRA. "These data give us confidence to advance TYRA-300 through Part B in SURF301 and explore larger opportunities with Phase 2 studies in metastatic urothelial cancer, non-muscle invasive bladder cancer and achondroplasia."

ENA 2024 presentation details:

Title: "*Preliminary safety and anti-tumor activity of TYRA-300, a highly selective FGFR3 inhibitor, in participants with advanced solid tumors with activating FGFR3 mutations/fusions (SURF301)*"

Session: Late Breaking Abstracts and Proffered Papers: Novel discoveries in drug development
Date: Friday, October 25, 2024
Time: 15:36 - 15:48 hrs CEST
Abstract #: 500LBA

Conference Call Information

TYRA is hosting a conference call and webcast on October 25, 2024, at 8am ET to review the interim clinical proof-of-concept results demonstrated with TYRA-300 in mUC. Participants may access a live webcast of the call and the associated slide presentation on the "For Investors" page of the TYRA website at https://ir.tyra.bio. To participate via telephone, please register in advance at this **link**. Upon registration, all telephone participants will receive a confirmation email detailing how to join the conference call, including the dial-in number along with a unique passcode and registrant ID that can be used to access the call. A replay of the conference call and webcast will be archived on the Company's website for at least 30 days.

About TYRA-300 and the SURF301 Study

TYRA-300 is TYRA's lead precision medicine program stemming from its in-house SNÅP platform. TYRA-300 is an investigational, oral, FGFR3-selective inhibitor currently in development for the treatment of cancer and skeletal dysplasias, including achondroplasia and hypochondroplasia. In oncology, TYRA-300 is being evaluated in a multi-center, open label Phase 1/2 clinical study, SURF301 (**S**tudy in **U**ntreated and **R**esistant **F**GFR3+ Advanced Solid Tumors) (NCT05544552). The study is designed to determine the optimal and the recommended Phase 2 dose (RP2D) of TYRA-300, as well as to evaluate the preliminary anti-tumor activity of TYRA-300. Part A of the study included patients with all solid tumors who are FGFR3 +/-, and explored doses of TYRA-300 ranging from 10mg -120mg once-daily (QD). Part A of SURF301 is complete. The Company continues to advance TYRA-300 through dose expansion in Part B, which includes patients with solid tumors who are $FGFR3^{+}$, to evaluate potentially therapeutic doses in preparation for potential future Phase 2 studies in metastatic urothelial carcinoma (mUC) and non-muscle invasive bladder cancer (NMIBC).

In skeletal dysplasias, TYRA-300 has demonstrated positive preclinical results in achondroplasia and hypochondroplasia. In July 2023 and January 2024, the FDA granted Orphan Drug Designation (ODD) and Rare Pediatric Designation (RPD) to TYRA-300, respectively, for the treatment of achondroplasia.

About Tyra Biosciences

Tyra Biosciences, Inc. (Nasdaq: TYRA) is a clinical-stage biotechnology company focused on developing next-generation precision medicines that target large opportunities in FGFR biology. The Company's in-house precision medicine platform, SNÅP, enables rapid and precise drug design through iterative molecular SNÅPshots that help predict genetic alterations most likely to cause acquired resistance to existing therapies. TYRA's expertise in FGFR biology has created a differentiated pipeline with three clinical-stage programs in targeted oncology and genetically defined conditions. The Company's lead precision medicine stemming from SNÅP, TYRA-300, is a potential first-in-class selective FGFR3 inhibitor that is designed to avoid the toxicities associated with inhibition of FGFR1, FGFR2 and FGFR4, while being agnostic for the FGFR3 gatekeeper mutations. TYRA-300 is in development for the treatment of cancer in the SURF301 Phase 1/2 study and for skeletal dysplasias, including achondroplasia and hypochondroplasia. TYRA is also developing TYRA-200, an investigational, FGFR1/2/3 inhibitor, in the

SURF201 study for metastatic intrahepatic cholangiocarcinoma, and TYRA-430, an investigational FGFR4/3-biased inhibitor for FGF19^{+}/FGFR4-driven cancers. TYRA is based in Carlsbad, CA.

For more information about our science, pipeline and people, please visit www.tyra.bio and engage with us on LinkedIn.

Forward-Looking Statements

TYRA cautions you that statements contained in this press release 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 to develop next-generation precision medicines and for TYRA-300 to be first-in-class, and the potential safety and therapeutic benefits of TYRA-300; the continued evaluation of TYRA-300 through Part B dose escalation in SURF301; the expected timing and phase of clinical development of TYRA-300; and the potential for SNÅP to develop therapies in targeted oncology and genetically defined conditions. Actual results may differ from those set forth in this press release 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 SNÅP 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.

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