Exelixis Announces Encouraging Results from Phase 1b/2 STELLAR-002 Trial Evaluating Zanzalintinib in Combination with Immune Checkpoint Inhibitors in Advanced Kidney Cancer at ASCO 2025

May 22, 2025

– Zanzalintinib in combination with nivolumab demonstrated an objective response rate of 63% and a disease control rate of 90% –

– Additional results from dose-finding cohorts will also be presented –

ALAMEDA, Calif.--(BUSINESS WIRE)--May 22, 2025-- Exelixis, Inc. (Nasdaq: EXEL) today announced results from an expansion cohort of the phase 1b/2 STELLAR-002 trial evaluating zanzalintinib in combination with either nivolumab (Opdivo®) or a fixed-dose combination of nivolumab and relatlimab (Opdualag™) in patients with previously untreated advanced clear cell renal cell carcinoma (RCC). These findings, as well as data from multiple dose-escalation cohorts from STELLAR-002, will be presented at the 2025 American Society of Clinical Oncology (ASCO) Annual Meeting.

“We are pleased to present these preliminary findings from the phase 1b/2 STELLAR-002 study, including early signs of promising activity for zanzalintinib in combination with immune checkpoint inhibitors,” said Amy Peterson, M.D., Executive Vice President, Product Development & Medical Affairs, and Chief Medical Officer, Exelixis. “Data emerging from this ongoing study are important to help inform further evaluation of zanzalintinib-based regimens in advanced solid tumors, including renal cell carcinoma.”

Abstract 4515: Zanzalintinib + Nivolumab ± Relatlimab in Patients with Previously Untreated Clear Cell Renal Cell Carcinoma: Results from an Expansion Cohort of the Phase 1b STELLAR-002 Study
Lead Author: Jad Chahoud, M.D., M.P.H., Moffitt Cancer Center, Tampa, Fla., USA
Session Title: Genitourinary Cancer—Kidney and Bladder
Saturday, May 31, 1:15-2:45 p.m. CDT

This expansion cohort of STELLAR-002 included patients with advanced clear cell RCC who received zanzalintinib in combination with either nivolumab (n=40) or fixed-dose nivolumab and relatlimab (n=40) in two non-randomized treatment arms. Patients had unresectable advanced or metastatic disease for which they received no prior systemic therapy. Intermediate- or poor-risk disease, per the International Metastatic RCC Database Consortium, accounted for 75% of patients receiving zanzalintinib in combination with nivolumab and 70% of patients receiving zanzalintinib in combination with fixed-dose nivolumab and relatlimab.

At a median follow-up of 20.1 months for those receiving zanzalintinib in combination with nivolumab and 15.9 months for those receiving zanzalintinib in combination with fixed-dose nivolumab and relatlimab, the objective response rates were 63% (95% confidence interval [CI]: 46-77%) and 40% (95% CI: 25-57%), respectively. Disease control rates were 90% (95% CI: 76-97%) for both arms. The 12-month duration of response was 73.4% (95% CI: 50.0-87.1%) and 74.1% (95% CI: 39.1-90.9%), respectively. Median progression-free survival was 18.5 months (95% CI: 9.5 months-not estimable [NE]) and 13.0 months (95% CI: 7.4 months-NE), respectively.

“While significant progress has been made in advanced clear cell renal cell carcinoma, many patients still experience disease progression, and more effective therapies earlier in the treatment landscape are needed,” said Jad Chahoud, M.D., M.P.H., Associate Member, Department of Genitourinary Oncology and Medical Director of the Inpatient/Outpatient (IPOP) service at Moffitt Cancer Center in Tampa, Fla., who is presenting the findings. “The high rate of durable responses and long progression-free survival observed for zanzalintinib in combination with nivolumab are encouraging and support further evaluation of this regimen.”

Treatment-emergent adverse events (TEAEs) of any grade were reported in all patients. Grade 3/4 TEAEs occurring in at least four patients receiving zanzalintinib in combination with nivolumab included hypertension (n=13), diarrhea (n=6), aspartate aminotransferase increase (n=5), alanine aminotransferase increase (n=5) and palmar-plantar erythrodysesthesia (n=4). Grade 3/4 TEAEs occurring in at least four patients receiving zanzalintinib in combination with fixed-dose nivolumab and relatlimab included hypertension (n=6), rash (n=6), lipase increase (n=4) and pulmonary embolism (n=4). There were two grade 5 TEAEs in each arm; none were considered related to study treatment. Three patients (8%) in the zanzalintinib in combination with nivolumab arm and eight patients (20%) in the zanzalintinib in combination with fixed-dose nivolumab and relatlimab arm discontinued all study drugs for treatment-related AEs as assessed by investigator.

Abstract 3101: Zanzalintinib + Nivolumab ± Relatlimab in Patients with Advanced Solid Tumors: Results from Two Dose-Escalation Cohorts of the Phase 1b STELLAR 002 Study
Lead Author: Benjamin Garmezy, M.D., Sarah Cannon Research Institute, Nashville, Tenn., USA
Session Title: Developmental Therapeutics—Molecularly Targeted Agents and Tumor Biology
Monday, June 2, 1:30-4:30 p.m. CDT

This analysis of STELLAR-002 included multiple cohorts of patients with advanced solid tumors who received zanzalintinib 100 mg in combination with nivolumab (n=19); zanzalintinib 60 mg in combination with fixed-dose nivolumab and relatlimab (n=24); or zanzalintinib 100 mg in combination with fixed-dose nivolumab and relatlimab (n=25). The most common cancer types for those receiving zanzalintinib in combination with nivolumab were colorectal and prostate cancers, followed by lung cancer and RCC. The most common tumor types in the zanzalintinib in combination with fixed-dose nivolumab and relatlimab cohorts were RCC, followed by prostate cancer, melanoma and colorectal cancer.

The findings showed that the toxicity profile of these combinations was manageable and consistent with each monotherapy agent. Preliminary safety, efficacy and pharmacokinetic results supported selection of the 100 mg dose for zanzalintinib for the ongoing expansion cohorts.

About STELLAR-002
STELLAR-002 (NCT05176483) is a global, open-label phase 1b/2 study of zanzalintinib as a single agent or in combination with nivolumab, fixed-dose nivolumab and relatlimab or nivolumab and ipilimumab in advanced solid tumors. The objective of the study is to evaluate the safety, tolerability and efficacy of zanzalintinib alone and in these combinations. The trial is divided into two parts: a dose-escalation stage and an expansion cohort stage. Expansion cohorts include patients with clear cell RCC, non-clear cell RCC, castration-resistant prostate cancer, urothelial carcinoma, hepatocellular carcinoma, non-small cell lung cancer, colorectal cancer and head and neck squamous cell carcinoma. Exelixis is sponsoring STELLAR-002, and Bristol Myers Squibb is providing nivolumab, ipilimumab and a fixed-dose combination of nivolumab and relatlimab for use in the trial. More information about the trial is available at ClinicalTrials.gov.

About Zanzalintinib
Zanzalintinib is a third-generation oral tyrosine kinase inhibitor that inhibits the activity of receptor tyrosine kinases implicated in cancer growth and spread, including VEGF receptors, MET, AXL and MER. These receptor tyrosine kinases are involved in both normal cellular function and in pathologic processes such as oncogenesis, metastasis, tumor angiogenesis and resistance to multiple therapies, including immune checkpoint inhibitors. With zanzalintinib, Exelixis sought to build upon its extensive experience with the target profile of cabozantinib, the company's flagship medicine, while improving key characteristics, including pharmacokinetic half-life. Zanzalintinib is currently being developed for the treatment of advanced solid tumors, including neuroendocrine tumors, genitourinary, colorectal and head and neck cancers.

About RCC
Kidney cancer is among the top ten most commonly diagnosed forms of cancer among both men and women in the U.S.[1] Nearly 81,000 Americans will be diagnosed with kidney cancer in 2025.[1] Clear cell RCC is the most common type of kidney cancer in adults.[2] Non-clear cell RCC represents about 25% of RCC cases, with fewer treatment options available and poorer outcomes compared with clear cell RCC.[3] Advanced or metastatic RCC occurs when the cancer has spread beyond the kidney.[4] If detected in its early stages, the five-year survival rate for RCC is high; for patients with advanced or late-stage metastatic RCC, however, the five-year survival rate is only 18%.[5] In 2025, approximately 33,700 patients with advanced kidney cancer will require systemic therapy in the U.S., with over 21,400 patients receiving first-line treatment.[6]

About Exelixis
Exelixis is a globally ambitious oncology company innovating next-generation medicines and regimens at the forefront of cancer care. Powered by drug discovery and development excellence, we are rapidly evolving our product portfolio to target an expanding range of tumor types and indications with our clinically differentiated pipeline of small molecules, antibody-drug conjugates and other biotherapeutics. This comprehensive approach harnesses decades of robust investment in our science and partnerships to advance our investigational programs and extend the impact of our flagship commercial product, CABOMETYX® (cabozantinib). Exelixis is driven by a bold scientific pursuit to create transformational treatments that give more patients hope for the future. For information about the company and its mission to help cancer patients recover stronger and live longer, visit www.exelixis.com, follow @ExelixisInc on X (Twitter), like Exelixis, Inc. on Facebook and follow Exelixis on LinkedIn.

Forward-Looking Statements
This press release contains forward-looking statements, including, without limitation, statements related to: the presentation of results from the Phase 1b/2 STELLAR-002 trial at ASCO 2025; the therapeutic potential of zanzalintinib in combination with either nivolumab or a fixed-dose combination of nivolumab and relatlimab in patients with previously untreated advanced clear cell RCC and advanced solid tumors; and Exelixis' scientific pursuit to create transformational treatments that give more patients hope for the future. Any statements that refer to expectations, projections or other characterizations of future events or circumstances are forward-looking statements and are based upon Exelixis' current plans, assumptions, beliefs, expectations, estimates and projections. Forward-looking statements involve risks and uncertainties. Actual results and the timing of events could differ materially from those anticipated in the forward-looking statements as a result of these risks and uncertainties, which include, without limitation: the availability of data at the referenced times; Exelixis' and Bristol Myers Squibb's continuing compliance with applicable legal and regulatory requirements; the potential failure of zanzalintinib in combination with either nivolumab or a fixed-dose combination of nivolumab and relatlimab to demonstrate safety and/or efficacy in future clinical testing; unexpected concerns that may arise as a result of the occurrence of adverse safety events or additional data analyses of clinical trials evaluating zanzalintinib; the costs of conducting clinical trials; Exelixis' dependence on third-party vendors for the development, manufacture and supply of zanzalintinib; Exelixis' ability to protect its intellectual property rights; market competition; changes in economic and business conditions; and other factors affecting Exelixis and its development programs detailed from time to time under the caption "Risk Factors" in Exelixis' most recent Annual Report on Form 10-K and subsequent Quarterly Reports on Form 10-Q, and in Exelixis' future filings with the Securities and Exchange Commission. All forward-looking statements in this press release are based on information available to Exelixis as of the date of this press release, and Exelixis undertakes no obligation to update or revise any forward-looking statements contained herein, except as required by law.

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[1] Cancer Facts & Figures 2025. ACS website. Available at: https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2025/2025-cancer-facts-and-figures-acs.pdf. Accessed May 2025.

[2] What Is Kidney Cancer? ACS website. Available at: https://www.cancer.org/cancer/kidney-cancer/about/what-is-kidney-cancer.html. Accessed May 2025.

[3] Bilen, M.A. Immune Checkpoint Inhibition in Advanced Non-Clear Cell Renal Cell Carcinoma: Leveraging Success from Clear Cell Histology into New Opportunities. *Cancers (Basel).* 2021;13(15):3652.

[4] Kidney Cancer. Cleveland Clinic. Available at: https://my.clevelandclinic.org/health/diseases/9409-kidney-cancer-overview. Accessed May 2025.

[5] Kidney Cancer Early Detection, Diagnosis, and Staging. ACS website. Available at: https://www.cancer.org/cancer/types/kidney-cancer/detection-diagnosis-staging.html. Accessed May 2025.

[6] Citeline's Datamonitor Healthcare: Renal Cell Carcinoma. March 2023 (internal data on file).

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