Exelixis Announces Detailed Results from Phase 3 STELLAR-303 Pivotal Trial Evaluating Zanzalintinib in Combination with an Immune Checkpoint Inhibitor in Metastatic Colorectal Cancer Presented at ESMO 2025 and Published in The Lancet

October 20, 2025

– Zanzalintinib in combination with atezolizumab improved median overall survival to 10.9 months versus 9.4 months with regorafenib, and significantly reduced the risk of death by 20% in the intention-to-treat population –

– Exelixis plans to complete its first new drug application submission for zanzalintinib in the U.S. in 2025 –

ALAMEDA, Calif.--(BUSINESS WIRE)--Oct. 20, 2025-- Exelixis, Inc. (Nasdaq: EXEL) today announced detailed results from STELLAR-303, a global phase 3 pivotal trial evaluating zanzalintinib in combination with atezolizumab (Tecentriq®) versus regorafenib in patients with previously treated non-microsatellite instability (MSI)-high metastatic colorectal cancer (CRC). As previously announced, the study met one of its dual primary endpoints, demonstrating a 20% reduction in the risk of death with the combination in the intention-to-treat (ITT) population at the final analysis (stratified hazard ratio [HR]: 0.80; 95% confidence interval [CI]: 0.69-0.93; P=0.0045). At a median follow-up of 18.0 months, median overall survival (OS) in the ITT population was 10.9 months with zanzalintinib in combination with atezolizumab versus 9.4 months with regorafenib. Detailed findings from the study, including OS and progression-free survival (PFS) in the ITT population and in the subset of patients without liver metastases, are being presented today at the 2025 European Society for Medical Oncology (ESMO) Congress during the Proffered Paper Session 2: GI Tumours, Lower Digestive at 9:25 a.m. CEST and simultaneously published in *The Lancet*.

“While treating non-MSI-high metastatic colorectal cancer remains a challenge, the combination of zanzalintinib and atezolizumab has shown consistent benefits across key subgroups of patients,” said Anwaar Saeed, M.D., Section Chief of Gastrointestinal Oncology at the University of Pittsburgh, Director of the Gastrointestinal Disease Center at UPMC Hillman Cancer Center and a lead investigator of the trial. “STELLAR-303 is the first immunotherapy-based phase 3 trial that demonstrated improved overall survival with a differentiated kinase inhibitor compared to a standard of care in this patient population. The survival benefit was demonstrated early and was consistent throughout the trial, underscoring the combination’s potential for patients in need of a new and effective treatment option after disease progression.”

An OS benefit with the combination was consistently observed across pre-specified subgroups, including geographic region, *RAS* status, liver involvement and prior anti-VEGF therapy, as presented in Table 1 below. The 12- and 24-month landmark OS estimates were 46% (95% CI: 41-51) and 20% (95% CI: 15-26), respectively, for the combination of zanzalintinib and atezolizumab, and 38% (95% CI: 34-43) and 10% (95% CI: 6-16), respectively, for regorafenib.

TABLE 1	Median OS, months (95% CI)		HR (95% CI)
	Zanzalintinib + Atezolizumab	Regorafenib	
Geographic region			
Asia	11.5 (9.2-13.7)	8.8 (7.8-10.4)	0.77 (0.59-1.00)
Rest of the world	10.9 (9.3-12.3)	9.8 (8.3-10.9)	0.82 (0.68-0.99)
***RAS* status**			
Wild type	12.0 (10.1-14.6)	10.4 (8.7-12.3)	0.79 (0.61-1.01)
Mutant	10.3 (9.0-11.9)	8.7 (8.1-9.8)	0.80 (0.66-0.98)
Active liver metastases			
Presence	8.9 (8.0-9.9)	7.7 (6.5-8.5)	0.78 (0.65-0.94)
Absence	15.9 (13.5-17.6)	12.8 (10.9-15.5)	0.77 (0.59-1.01)
Prior anti-VEGF antibody treatment			
Yes	10.6 (9.3-12.5)	8.8 (8.3-9.9)	0.80 (0.68-0.95)
No	11.5 (8.7-13.5)	11.1 (9.5-12.6)	0.80 (0.56-1.15)

OS = overall survival; CI = confidence interval; HR = hazard ratio; VEGF = vascular endothelial growth factor

Data pertaining to the other dual primary endpoint, OS in patients without liver metastases (non-liver metastases, NLM), were immature at the data cutoff. A prespecified interim analysis showed a trend in OS favoring the combination (15.9 months versus 12.8 months; stratified HR: 0.79; 95% CI: 0.61-1.03; P=0.0875) at a median follow-up of 16.8 months. The trial will proceed to the planned final analysis for this endpoint.

“These detailed results from STELLAR-303 provide further insight into the combination of zanzalintinib and atezolizumab as a potential new option to extend survival in patients with previously treated metastatic colorectal cancer,” said Dana T. Aftab, Ph.D., Executive Vice President, Research and Development, Exelixis. “Before the end of this year, we intend to complete the submission of our first new drug application for zanzalintinib as we work toward bringing this combination regimen to a patient community seeking a new and chemotherapy-free option. These data, along with our robust clinical trial program, underscore the progress we are making toward our goal of increasing the scope and scale of the solid tumor types zanzalintinib may help address.”

A trend for improvement in PFS with the combination was also observed in the ITT population (stratified HR: 0.68 [95% CI: 0.59–0.79]; median, 3.7 [95% CI: 3.5–3.8] months versus 2.0 [95% CI: 1.9–2.6] months), though statistical superiority cannot be claimed at this time due to the prespecified

hierarchical testing strategy. The trend for PFS improvement with zanzalintinib in combination with atezolizumab versus regorafenib was consistent across subgroups.

The safety profiles of zanzalintinib in combination with atezolizumab and of regorafenib were generally consistent with what has been previously observed, and no new safety signals were identified. Grade 3/4 treatment-related adverse events (AEs) occurred in 59% of patients receiving zanzalintinib in combination with atezolizumab and 37% of patients receiving regorafenib. AEs leading to discontinuation of all study treatment occurred in 18% versus 15% of patients, respectively. The most common grade 3/4 treatment-related AEs were hypertension (15% versus 9%, respectively), fatigue (6% versus 2%), diarrhea (6% versus 2%) and proteinuria (6% versus 2%). Deaths considered related to treatment by investigators were two for zanzalintinib, two for atezolizumab, one for the combination and one for regorafenib.

About STELLAR-303
STELLAR-303 (NCT05425940) is a global, multicenter, randomized, phase 3, open-label study that randomized patients 1:1 to either zanzalintinib in combination with atezolizumab (n=451) or regorafenib (n=450). The study includes patients with previously treated non-MSI-high metastatic CRC. The dual primary endpoints of the study are OS in the ITT population and in the NLM subgroup of patients. The ITT population consisted of all randomized patients, regardless of the presence of liver metastases. The NLM subgroup consisted of patients who did not have active liver metastases at baseline as determined by investigator assessment. Secondary endpoints include PFS, objective response rate and duration of response in the ITT population and in the NLM subgroup of patients. More information about the trial is available at ClinicalTrials.gov.

About Zanzalintinib
Zanzalintinib is a novel oral kinase inhibitor that inhibits the activity of the TAM kinases (TYRO3, AXL, MER), MET and VEGF receptors. These kinases play important roles in oncogenic processes including tumor cell proliferation, metastasis, angiogenesis, drug resistance and evasion of antitumor immunity. 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 colorectal cancer, kidney cancer and neuroendocrine tumors.

Zanzalintinib is an investigational agent that is not approved for any use and is the subject of ongoing clinical trials.

About CRC
CRC is the third most common cancer and the second leading cause of cancer-related deaths in the U.S.[1] Approximately 154,000 new cases will be diagnosed in the U.S. with around 53,000 expected deaths from the disease in 2025.[1] CRC is most frequently diagnosed among people aged 65-74 and is more common in men and in people of non-Hispanic American Indian/Alaska Native descent.[2] Nearly a quarter of CRC cases are diagnosed at the metastatic stage, at which point the five-year survival rate is just 16.2%.[2] The liver is the most common site for CRC metastasis. Liver metastases significantly impact survival, with a median five-year survival rate of less than 14% when treated with palliative chemotherapy.[3]

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 and 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 detailed results from the STELLAR-303 pivotal trial at ESMO 2025; the therapeutic potential of zanzalintinib in combination with atezolizumab to become a new and effective treatment option to extend survival for patients with previously treated metastatic CRC; Exelixis' plans to complete a new drug application submission for zanzalintinib in the U.S. in 2025; Exelixis' progress in clinical trials towards the goal of increasing the scope and scale of solid tumor types zanzalintinib may address; 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; complexities and the unpredictability of the regulatory review and approval processes in the U.S. and elsewhere; Exelixis' continuing compliance with applicable legal and regulatory requirements; unexpected concerns that may arise as a result of the occurrence of adverse safety events or additional data analyses of clinical trials evaluating zanzalintinib; 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.

---

[1] Key Statistics for Colorectal Cancer. ACS website. Available at: https://www.cancer.org/cancer/types/colon-rectal-cancer/about/key-statistics.html. Accessed October 2025.

[2] Cancer Stat Facts: Colorectal Cancer. SEER website. Available at: https://seer.cancer.gov/statfacts/html/colorect.html. Accessed October 2025.

[3] Ros J, Salva F, Dopazo C, et al. Liver transplantation in metastatic colorectal cancer: are we ready for it? *Br J Cancer.* May 2023;128(10):1797-1806.

View source version on businesswire.com: https://www.businesswire.com/news/home/20251015179453/en/

Investors Contact:
Susan Hubbard
EVP, Public Affairs and
Investor Relations
Exelixis, Inc.
650-837-8194
shubbard@exelixis.com

Media Contact:
Stekki Millman
Senior Director, Public Affairs
Exelixis, Inc.
650-837-7187
smillman@exelixis.com

Source: Exelixis, Inc.