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Exelixis and Natera to Collaborate on STELLAR-316, a Phase 3 Pivotal Trial of Zanzalintinib for Patients with Colorectal Cancer

– STELLAR-316 will use Natera's Signatera™ assay to identify MRD-positive patients for trial enrollment and to monitor response to therapy –

ALAMEDA, Calif. and AUSTIN, Texas – January 7, 2026 – Exelixis, Inc. (Nasdaq: EXEL) and Natera (Nasdaq: NTRA), a global leader in cell-free DNA and precision medicine, today announced their collaboration on the planned Exelixis-sponsored STELLAR-316 trial. This randomized phase 3 pivotal trial will evaluate zanzalintinib, Exelixis' novel oral kinase inhibitor, with and without an immune checkpoint inhibitor, in patients with resected stage II/III colorectal cancer (CRC).

Using Natera's Signatera™ test following completion of definitive therapy[1], patients with CRC who test positive for molecular residual disease (MRD) and have no radiographic evidence of disease will be eligible for enrollment in the STELLAR-316 trial. Working with patients and their providers, this trial will be fully enrolled with patients who are receiving commercial Signatera testing as part of their routine standard of care.

The primary endpoint of STELLAR-316 is disease-free survival. Signatera will also be used for longitudinal monitoring of circulating tumor DNA clearance, one of the secondary endpoints of the trial. Exelixis expects to initiate STELLAR-316 in mid-2026.

[1]Colon: adjuvant chemotherapy, rectal: total neoadjuvant therapy

CRC is the third most common cancer and the second leading cause of cancer-related deaths in the U.S.[2] Of the approximately 89,000 stage II/III colorectal cancer cases projected for 2035,[3] about 20% of these patients are expected to remain MRD-positive following definitive therapy.[3] Patients with stage II/III CRC who are MRD-positive have been shown to experience worse outcomes in multiple clinical studies[4,5,6] and there are no established or approved therapies for this specific patient population in the U.S.

"Patients with colorectal cancer who are MRD-positive following definitive therapy face a high risk of recurrence, underscoring the urgent need for new treatment options that can help prevent clinical metastatic progression," said Dana T. Aftab, Ph.D., Executive Vice President, Research and Development, Exelixis. "STELLAR-316 is our second pivotal trial of zanzalintinib in patients with CRC and represents our continued commitment to addressing unmet needs in this patient population by conducting rigorous trials with the potential to improve standards of care. We are excited to collaborate with Natera on STELLAR-316, which, if successful, could make zanzalintinib the first MRD-guided treatment for these patients."

"Exelixis and Natera's collaboration on STELLAR-316 underscores both companies' commitment to advancing new approaches to treat CRC," said John Simmons, Ph.D., Global Vice President, Biopharma, Natera. "Leveraging Signatera to inform trial enrollment will help to identify high-risk patients earlier, enabling intervention when disease burden is lower – and importantly, with the potential to improve clinical outcomes."

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.

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[2]Key Statistics for Colorectal Cancer. ACS website. Available at: https://www.cancer.org/cancer/types/colon-rectal-cancer/about/key-statistics.html. Accessed January 2026.

[3]Decision Resource Group. Diagnosed stage II/III CRC incident cases in 2035

[4]Shah PK et al. Circulating tumor DNA for Detection of Molecular Residual Disease (MRD) in Patients with Stage II/III Colorectal Cancer (CRC): Final Analysis of the BESPOKE CRC Sub cohort, presented at the 2025 ASCO GI.

[5]Cohen SA, et al. Real-world monitoring of ctDNA reliably predicts cancer recurrence and treatment efficacy in patients. Ann Surg. Published online August 7, 2025. doi:10.1097/SLA.0000000000006887.

[6]Nakamura, Y., Watanabe, J., Akazawa, N. et al., ctDNA-based molecular residual disease and survival in resectable colorectal cancer. Nat Med (2024).

Exelixis recently confirmed it has submitted a New Drug Application to the U.S. Food & Drug Administration for zanzalintinib for the treatment of patients with previously treated metastatic colorectal cancer, when used in combination with atezolizumab (Tecentriq®). The regulatory filing was based on positive results from the phase 3 STELLAR-303 pivotal trial, which met one of its dual primary endpoints, with the combination of zanzalintinib and atezolizumab demonstrating a statistically significant reduction in the risk of death versus regorafenib in the intention-to-treat population at the final analysis. An overall survival (OS) benefit with the combination was consistently observed across pre-specified subgroups, including geographic region, RAS status, liver involvement and prior anti-VEGF therapy. Data pertaining to the other dual primary endpoint, OS in patients without liver metastases (non-liver metastases or NLM), were immature at the data cutoff. A prespecified interim analysis showed a trend in OS favoring the combination. The trial will proceed to the planned final analysis for this endpoint, which is expected in mid-2026, based on current event rates.

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.[7] Nearly a quarter of CRC cases are diagnosed at the metastatic stage, at which point the five-year survival rate is just 16.2%.[6] 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.[8]

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

[7]Cancer Stat Facts: Colorectal Cancer. SEER website. Available at: https://seer.cancer.gov/statfacts/html/colorect.html. Accessed January 2026.

[8]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.

stronger and live longer, visit www.exelixis.com, follow @ExelixisInc on X (Twitter), like Exelixis, Inc. on Facebook and follow Exelixis on LinkedIn.

About Natera

Natera™ is a global leader in cell-free DNA and precision medicine, dedicated to oncology, women's health, and organ health. We aim to make personalized genetic testing and diagnostics part of the standard-of-care to protect health and inform earlier, more targeted interventions that help lead to longer, healthier lives. Natera's tests are supported by more than 325 peer-reviewed publications that demonstrate excellent performance. Natera operates ISO 13485-certified and CAP-accredited laboratories certified under the Clinical Laboratory Improvement Amendments (CLIA) in Austin, Texas, and San Carlos, California, and through Foresight Diagnostics, its subsidiary, operates an ISO 27001-certified and CAP-accredited laboratory certified under CLIA in Boulder, Colorado. For more information, visit www.natera.com.

Exelixis Forward-Looking Statements

This press release contains forward-looking statements, including, without limitation, statements related to: Exelixis' clinical development plans for zanzalintinib, including in collaboration with Natera for the phase 3 pivotal trial STELLAR-316; Exelixis's belief in the therapeutic potential of zanzalintinib, including the potential to be the first MRD-guided treatment for patients with CRC; Exelixis' commitment to addressing unmet needs in patients with CRC by conducting rigorous trials with the potential to improve standards of care; 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 potential failure of zanzalintinib to demonstrate safety and/or efficacy in clinical trials; complexities and the unpredictability of the regulatory review and approval processes in the U.S. and elsewhere; Exelixis' and Natera's continuing compliance with applicable legal and regulatory requirements; the costs of conducting clinical trials; Exelixis' dependence on third-party vendors for the development, manufacture and supply of zanzalintinib; Exelixis' and Natera's 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.

Natera Forward-Looking Statements

All statements other than statements of historical facts contained in this press release are forward-looking statements and are not a representation that Natera's plans, estimates, or expectations will be achieved. These forward-looking statements represent Natera's expectations as of the date of this press release, and Natera disclaims any obligation to update the forward-looking statements. These forward-looking statements are subject to known and unknown risks and uncertainties that may cause actual results to differ materially, including with respect to whether the results of clinical or other studies will support the use of our product offerings, the impact of results of such studies, our expectations of the reliability, accuracy and performance of our tests, or of the benefits of our tests and product offerings to patients, providers and payers. Additional risks and uncertainties are discussed in greater detail in "Risk Factors" in Natera's recent filings on Forms 10-K and 10-Q and in other filings Natera makes with the SEC from time to time. These documents are available at www.natera.com/investors and www.sec.gov.

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