



Exelixis Announces Initiation of the STELLAR-304 Phase 3 Pivotal Trial Evaluating Zanzalintinib in Patients with Advanced Non-Clear Cell Kidney Cancer

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– STELLAR-304 is the second phase 3 pivotal trial evaluating zanzalintinib, a next-generation tyrosine kinase inhibitor in development for multiple advanced tumor types –

ALAMEDA, Calif.--(BUSINESS WIRE)--Dec. 22, 2022-- [Exelixis, Inc.](#) (Nasdaq: EXEL) today announced the initiation of STELLAR-304, a phase 3 pivotal trial evaluating zanzalintinib in combination with nivolumab versus sunitinib in patients with advanced non-clear cell renal cell carcinoma (nccRCC). Zanzalintinib, which was adopted as the generic name for XL092, is a next-generation tyrosine kinase inhibitor (TKI) in development for multiple advanced tumor types.

"In September at ESMO 2022, we presented zanzalintinib phase 1 data which demonstrated promising clinical activity across a range of tumors with a manageable safety profile. We were particularly encouraged by the activity of zanzalintinib in advanced kidney cancer patients, including patients with non-clear cell subtypes. Based on this zanzalintinib data and given that nivolumab has shown activity in non-clear cell kidney cancer, we are excited to evaluate this combination regimen in this population in STELLAR-304," said Vicki L. Goodman, M.D., Executive Vice President, Product Development & Medical Affairs, and Chief Medical Officer, Exelixis. "STELLAR-304 is the first and only randomized controlled phase 3 study to focus specifically across non-clear cell renal cell carcinoma subtypes, a patient population with limited clinical data and poorer treatment outcomes. We look forward to continuing our legacy of working towards improving care for all kidney cancer patients."

STELLAR-304 is a global, multicenter, randomized phase 3 open-label study that will enroll approximately 291 patients with unresectable, locally advanced or metastatic nccRCC with no prior systemic anticancer therapy. One prior systemic adjuvant therapy, including immune checkpoint inhibitor (ICI) therapy and excluding sunitinib, is allowed for completely resected RCC and if recurrence occurred at least six months after the last dose of adjuvant therapy. Patients will be randomized 2:1 to receive either zanzalintinib in combination with nivolumab or sunitinib monotherapy. The primary objective of the study is to evaluate the efficacy of the combination, as measured by duration of progression-free survival and objective response rate per Response Evaluation Criteria in Solid Tumors version 1.1 as assessed by the Blinded Independent Radiology Committee. The secondary endpoint is duration of overall survival.

STELLAR-304 is sponsored by Exelixis, and Bristol Myers Squibb is providing nivolumab for the trial.

About Zanzalintinib (XL092)

Zanzalintinib is a next-generation oral TKI 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 ICIs. In designing 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 genitourinary cancers, as a monotherapy and in combination with ICIs.

About RCC

The American Cancer Society's 2022 statistics cite kidney cancer as among the top 10 most commonly diagnosed forms of cancer among both men and women in the U.S.¹ Clear cell RCC is the most common type of kidney cancer in adults.² nccRCC represents about 20-25% of RCC cases, with fewer treatment options available and poorer outcomes compared with clear cell RCC.³ If RCC is detected in its early stages, the five-year survival rate is high; for patients with advanced or late-stage metastatic RCC, however, the five-year survival rate is only 14%.¹ Approximately 33,000 patients in the U.S. and more than 71,000 worldwide will require systemic treatment for advanced kidney cancer in 2022, with over 15,000 patients in need of a first-line treatment in the U.S.⁴

About Exelixis

Founded in 1994, Exelixis, Inc. (Nasdaq: EXEL) is a commercially successful, oncology-focused biotechnology company that strives to accelerate the discovery, development and commercialization of new medicines for difficult-to-treat cancers. Following early work in model system genetics, we established a broad drug discovery and development platform that has served as the foundation for our continued efforts to bring new cancer therapies to patients in need. Our discovery efforts have resulted in four commercially available products, CABOMETYX[®] (cabozantinib), COMETRIQ[®] (cabozantinib), COTELLIC[®] (cobimetinib) and MINNEBRO[®] (esaxerenone), and we have entered into partnerships with leading pharmaceutical companies to bring these important medicines to patients worldwide. Supported by revenues from our marketed products and collaborations, we are committed to prudently reinvesting in our business to maximize the potential of our pipeline. We are supplementing our existing therapeutic assets with targeted business development activities and internal drug discovery – all to deliver the next generation of Exelixis medicines and help patients recover stronger and live longer. Exelixis is a member of the Standard & Poor's (S&P) MidCap 400 index, which measures the performance of profitable mid-sized companies. For more information about Exelixis, please visit www.exelixis.com, follow [@ExelixisInc](https://twitter.com/ExelixisInc) on Twitter or like [Exelixis, Inc.](https://www.facebook.com/ExelixisInc) on Facebook.

Forward-Looking Statements

This press release contains forward-looking statements, including, without limitation, statements related to: the clinical and therapeutic potential of zanzalintinib in combination with nivolumab as a treatment for patients with advanced nccRCC; and Exelixis' plans to reinvest in its business to maximize the potential of the company's pipeline, including through targeted business development activities and internal drug discovery. 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 the combination of zanzalintinib and nivolumab to demonstrate safety and/or efficacy in STELLAR-304; uncertainties inherent in the product development process; 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; the continuing COVID-19 pandemic and other global events and their impact on Exelixis' research and development operations, including Exelixis' ability to initiate new clinical trials and clinical trial sites, enroll clinical trial patients, conduct trials per protocol, and conduct drug research and discovery operations and related activities; 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 discussed under the caption "Risk Factors" in Exelixis' Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission (SEC) on November 1, 2022, and in Exelixis' future filings with the SEC. 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 American Cancer Society: Cancer Facts & Figures 2022. Available at: <https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2022/2022-cancer-facts-and-figures.pdf>. Accessed December 2022.

² Jonasch, E., Gao, J., Rathmell, W., Renal cell carcinoma. *BMJ*. 2014; 349:g4797.

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 Decision Resources Report: Renal Cell Carcinoma. October 2014 (internal data on file).

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Investors:

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

Media:

Lindsay Treadway
Executive Director, Public Affairs
and Advocacy Relations
Exelixis, Inc.
(650) 837-7522
ltreadway@exelixis.com

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