Exelixis and Insilico Medicine Enter into Exclusive Global License Agreement for ISM3091, a Potentially Best-in-Class USP1 Inhibitor

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—ISM3091 is a highly selective, orally bioavailable small molecule inhibitor of USP1 identified through Insilico Medicine's artificial intelligence (AI) platform, with potent activity in BRCA-mutated tumor models —

—In April 2023, the U.S. Food and Drug Administration (FDA) cleared Insilico's Investigational New Drug application (IND) for ISM3091 in patients with solid tumors —

ALAMEDA, Calif. & NEW YORK--(BUSINESS WIRE)--Sep. 12, 2023-- Exelixis, Inc. (Nasdaq: EXEL) and Insilico Medicine ("Insilico") today announced that the companies have entered into an exclusive license agreement granting Exelixis global rights to develop and commercialize ISM3091, a potentially best-in-class small molecule inhibitor of USP1, which has emerged as a synthetic lethal target in the context of BRCA-mutated tumors.

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Under the terms of the agreement, Insilico granted Exelixis an exclusive, worldwide license to develop and commercialize ISM3091, and other USP1-targeting compounds, in exchange for an upfront payment to Insilico of $80 million anticipated in the third quarter 2023. Insilico is also eligible to receive future development, commercial, and sales-based milestone payments, as well as tiered royalties on net sales.

"ISM3091 represents a potentially best-in-class approach to inhibiting USP1, an important oncology target with broad applicability in BRCA-mutant tumors," said Dana Aftab, Ph.D., Executive Vice President, Discovery and Translational Research and Chief Scientific Officer, Exelixis. "We believe preclinical data on ISM3091's potent anti-tumor activity, tolerability, and pharmacokinetics set the compound apart from competing USP1 inhibitors and make it an important addition to Exelixis' growing clinical-stage pipeline. Following the FDA's clearance of Insilico's IND earlier this spring, we're looking forward to accelerating phase 1 trial enrollment."

"ISM3091 is the third clinical-stage program made possible by Chemistry42, Insilico Medicine's generative AI platform for small molecule drug discovery," said Alex Zhavoronkov, Ph.D., founder and CEO of Insilico Medicine. "The compound's novel structure, anti-tumor activity, and excellent drug-like properties give it significant potential as a differentiated program directed at BRCA-mutant tumors, which include forms of ovarian, prostate, and breast cancer. This program attracted significant interest from multiple potential partners in the pharmaceutical industry, but we were most impressed by the level of technical expertise and development and commercial capabilities of Exelixis. With a track record of commercial and clinical development success in oncology, Exelixis is the best partner to take ISM3091 forward, and we're excited to see the program take flight as a component of the company's pipeline behind cabozantinib, its global oncology franchise."

USP1 facilitates DNA damage repair by removing ubiquitin from multiple substrates including proteins that stabilize the replication fork. A small molecule discovered using Insilico Medicine's generative AI platform with extensive multiparameter optimization capabilities, ISM3091 was designed to inhibit the activity of USP1. In preclinical experiments, ISM3091 was found to be potently efficacious against multiple tumor cell lines and *in vivo* models with BRCA mutations, as well as in homologous recombination DNA repair (HRR)-proficient models, both as a single agent and in combination with PARP inhibitors. It is also well tolerated in different species with a high margin of safety. Insilico disclosed select data in a poster presentation at the American Association for Cancer Research Annual Meeting in April 2023. On April 17, 2023, the FDA cleared the initial IND for ISM3091 for the treatment of patients with solid tumors.

About Insilico Medicine

Insilico Medicine, a global clinical stage biotechnology company powered by generative AI, is connecting biology, chemistry, and clinical trials analysis using next-generation AI systems. The company has developed AI platforms that utilize deep generative models, reinforcement learning, transformers, and other modern machine learning techniques for novel target discovery and the generation of novel molecular structures with desired properties. Insilico Medicine is developing breakthrough solutions to discover and develop innovative drugs for cancer, fibrosis, immunity, central nervous system diseases, infectious diseases, autoimmune diseases, and aging-related diseases. www.insilico.com

About Exelixis

Exelixis is a globally ambitious oncology company innovating next-generation medicines and regimens at the forefront of cancer care. Powered by bi-coastal centers of 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, like Exelixis, Inc. on Facebook and follow Exelixis on LinkedIn.

Exelixis Forward-Looking Statements

This press release contains forward-looking statements, including, without limitation, statements related to: Exelixis' belief that ISM3091 is a potentially best-in-class small molecule inhibitor of USP1 with broad applicability in BRCA-mutated tumors, and that ISM3091's anti-tumor activity, tolerability and pharmacokinetics differentiate it from competing USP1 inhibitors and make it an important addition to Exelixis' growing clinical-stage pipeline; Exelixis' immediate and future financial and other obligations under the exclusive license agreement with Insilico, including the anticipated timing of Exelixis' payment of an $80 million upfront fee to Insilico; Exelixis' plans to accelerate phase 1 trial enrollment; 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 level of costs associated with Exelixis' commercialization, research and development, in-licensing or acquisition of product candidates, and other activities; uncertainties inherent in the drug discovery and product development process; Exelixis' dependence on its relationship with Insilico, including Insilico's adherence to its obligations under the exclusive license agreement; complexities and the unpredictability of the regulatory review and approval processes in the U.S. and elsewhere; Exelixis' and Insilico's continuing compliance with applicable legal and regulatory requirements; Exelixis' and Insilico's ability to protect their respective intellectual property rights; market competition; changes in economic and business conditions; and other factors affecting Exelixis and its product pipeline discussed under the caption "Risk Factors" in Exelixis' Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission (SEC) on August 1, 2023 and Annual Report on Form 10-K filed with the SEC on February 7, 2023, 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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Exelixis Investors Contact:
Susan Hubbard
EVP, Public Affairs & Investor Relations
Exelixis, Inc.
650-837-8194
shubbard@exelixis.com

Exelixis Media Contact:
Hal Mackins
For Exelixis, Inc.
415-994-0040
hal@torchcommunications.com

Insilico Media Contact:
Brita Belli
Head of PR
Insilico Medicine
475-225-0843
brita@insilico.com

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