Erasca Announces First Patient Dosed in HERKULES-3, a Phase 1b/2 Gastrointestinal Cancer Master Protocol Evaluating ERAS-007 in Multiple Combinations

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ERAS-007, a potential best-in-class ERK1/2 inhibitor, will be evaluated initially in combinations that could address over half of patients with colorectal cancer

SAN DIEGO, Sept. 22, 2021 (GLOBE NEWSWIRE) -- Erasca, Inc. (Nasdaq: ERAS), a clinical-stage precision oncology company singularly focused on discovering, developing, and commercializing therapies for patients with RAS/MAPK pathway-driven cancers, today announced dosing of the first patient in HERKULES-3, a Phase 1b/2 master protocol clinical trial evaluating ERAS-007 in combination with various agents in patients with gastrointestinal (GI) cancer, with initial focus on patients with advanced colorectal cancer (CRC).

"A major barrier to durable responses with current treatment regimens for GI cancers is the emergence of resistance mechanisms, which are often associated with reactivation of the MAPK pathway," said Jonathan E. Lim, M.D., Erasca's chairman, CEO, and co-founder. "We have developed HERKULES-3, our GI master protocol, to evaluate ERAS-007 in rational combinations to assess the possibility of reducing susceptibility to resistance and increasing durability of treatment. Initially focused on CRC subtypes with BRAF V600E, KRAS, or NRAS mutations, HERKULES-3 has the potential to address over half of patients with CRC and could be further expanded into other GI cancers with additional combinations."

Approximately 10% of all patients with CRC have tumors that harbor a BRAF V600E mutation, with the majority developing rapid progression within four months due to resistance following initiation of the current standard of care treatment, the combination of encorafenib and cetuximab, which was approved in April 2020 for previously treated patients with BRAF V600E-mutant metastatic CRC (mCRC). Another 45-50% of CRC patients have tumors that harbor KRAS or NRAS mutations, for which there is currently no approved targeted therapeutic option.

Dr. Lim continued, "Preclinical work by Ryan Corcoran, M.D., Ph.D., at Massachusetts General Hospital Cancer Center indicates that adding an ERK inhibitor has the potential to deepen and prolong responses, as well as delay resistance, forming the scientific basis for exploring ERAS-007 in combination with encorafenib and cetuximab in patients with BRAF V600E-mutant mCRC. Additionally, Scott Kopetz, M.D., Ph.D., of MD Anderson Cancer Center presented compelling evidence at the AACR conference this year that CDK4/6 inhibition combined with MEK inhibition had the best *in vivo* efficacy across KRAS mutations. We evolved this one step further based on our preclinical data demonstrating superior efficacy with an ERK inhibitor in place of a MEK inhibitor, forming the scientific rationale for evaluating the highly promising and novel combination of ERAS-007 with the CDK4/6 inhibitor palbociclib in patients with mCRC driven by KRAS and NRAS mutations. We believe both combinations offer robust therapeutic potential in patients with high unmet need."

HERKULES-3 will examine the safety, tolerability, and preliminary efficacy of ERAS-007 in combination with other cancer therapies in study participants with GI malignancies. The dose escalation portions of the first two sub-studies will assess ERAS-007 in combination with the current standard of care, encorafenib (Braftovi®) and cetuximab (Erbitux®), in patients with BRAF V600E-mutant mCRC, and ERAS-007 in combination with the CDK4/6 inhibitor palbociclib (Ibrance®) in patients with KRAS- or NRAS-mutant mCRC. The Phase 2 dose expansion portion will further evaluate the safety and efficacy of each combination at the recommended dose identified in patients with previously treated mCRC. Future sub-studies of HERKULES-3 will explore ERAS-007 in combination with other agents in patients with different mutational subtypes of GI cancers.

About ERAS-007
ERAS-007 is a potential best-in-class ERK1/2 inhibitor being investigated alone or in combination with different inhibitors targeting upstream nodes of the MAPK pathway as part of Erasca's MAPKlamp strategy. The extracellular signal-regulated kinases (ERK), ERK1 and ERK2, belong to a family of serine-threonine kinases that regulate cellular signaling and comprise the terminal node of the RAS/MAPK pathway. The broad therapeutic potential of ERAS-007 is being investigated initially across four HERKULES clinical trials that span multiple tumor types and include both monotherapy and combinations with approved and investigational agents, such as RTK, SHP2, RAS, RAF, and/or cell cycle inhibitors. HERKULES-1, a Phase 1b/2 clinical trial for ERAS-007 as a single agent and in combination with the SHP2 inhibitor ERAS-601 (together, Erasca's first MAPKlamp) in advanced solid tumors, HERKULES-2, a Phase 1b/2 master protocol clinical trial for ERAS-007 in combination with various agents in patients with non-small cell lung cancer (NSCLC), and HERKULES-3, a Phase 1b/2 master protocol clinical trial for ERAS-007 in combination with various agents in patients with GI cancers, are currently enrolling patients. HERKULES-4, a Phase 1b/2 master protocol clinical trial for ERAS-007 in combination with various agents in patients with hematologic malignancies, is anticipated to begin in the first quarter of 2022.

About Erasca
At Erasca, our name is our mission: To erase cancer. We are a clinical-stage precision oncology company singularly focused on discovering, developing, and commercializing therapies for patients with RAS/MAPK pathway-driven cancers. Our company was co-founded by leading pioneers in precision oncology and RAS targeting to create novel therapies and combination regimens designed to comprehensively shut down the RAS/MAPK pathway for the treatment of cancer. We have assembled what we believe to be the deepest RAS/MAPK pathway-focused pipeline in the industry. We believe our team's capabilities and experience, further guided by our scientific advisory board which includes the world's leading experts in the RAS/MAPK pathway, uniquely position us to achieve our bold mission of erasing cancer.

Cautionary Note Regarding Forward-Looking Statements
Erasca cautions you that statements contained in this press release regarding matters that are not historical facts are forward-looking statements. The forward-looking statements are based on our current beliefs and expectations and include, but are not limited to: our expectations regarding the potential therapeutic benefits of our product candidates and the potential patient populations for our product candidates, including ERAS-007 and ERAS-601; and the planned advancement of our development pipeline, including the clinical development plans and anticipated start date for the

HERKULES-4 trial. Actual results may differ from those set forth in this press release due to the risks and uncertainties inherent in our business, including, without limitation: our approach to the discovery and development of product candidates based on our singular focus on shutting down the RAS/MAPK pathway, a novel and unproven approach; delays in our preclinical and clinical development programs; our dependence on third parties to conduct manufacturing, research, and preclinical and clinical testing; unexpected adverse side effects or inadequate efficacy of our product candidates that may limit their development, regulatory approval, and/or commercialization, or may result in recalls or product liability claims; unfavorable results from preclinical studies or clinical trials; results from preclinical studies or early clinical trials not necessarily being predictive of future results; regulatory developments in the United States and foreign countries; our ability to obtain and maintain intellectual property protection for our product candidates and maintain our rights under intellectual property licenses; our ability to fund our operating plans with our current cash, cash equivalents, and investments; our ability to maintain undisrupted business operations due to the COVID-19 pandemic; and other risks described in our prior filings with the Securities and Exchange Commission (SEC), including under the heading “Risk Factors” in our most recent quarterly report on Form 10-Q and any subsequent filings with the SEC. You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof, and we undertake no obligation to update such statements to reflect events that occur or circumstances that exist after the date hereof. All forward-looking statements are qualified in their entirety by this cautionary statement, which is made under the safe harbor provisions of the Private Securities Litigation Reform Act of 1995.

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