Erasca Announces Publication of Promising Clinical Data Supporting the Therapeutic Potential of Naporafenib in Combination with Trametinib in NRAS-Mutant Melanoma

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Promising preliminary antitumor activity with the combination demonstrated in heavily pretreated patients

47% ORR, 5.5 months mPFS observed with preferred combination dose of naporafenib 200 mg BID plus trametinib 1 mg QD

Dosing of first patient in Erasca's pivotal Phase 3 trial in NRASm melanoma (SEACRAFT-2) is expected in H1 2024

SAN DIEGO, April 25, 2023 (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 the publication of results in the *Journal of Clinical Oncology* from the expansion arm of a Phase 1b open label study evaluating pan-RAF inhibitor naporafenib plus MEK inhibitor trametinib (MEKINIST®) in patients with NRAS-mutant (NRASm) melanoma.

"These data support the promising anti-tumor potential of naporafenib in combination with trametinib in patients with NRASm melanoma. There are currently no approved targeted therapies for tumors with NRAS mutations, a mutation type associated with poor prognosis that afflicts about 20% of patients with melanoma," said Jonathan E. Lim, M.D., Erasca's chairman, CEO, and co-founder. "The post-immune checkpoint inhibitor setting is an area of high unmet medical need with the current standard of care being chemotherapy. The NEMO trial evaluating chemotherapy in patients with treatment-naïve NRASm melanoma demonstrated an objective response rate (ORR) of 7% and a median progression-free survival (mPFS) of 1.5 months. By comparison, the combination confirmed ORR of 47% and an mPFS of 5.5 months with 200 mg BID of naporafenib and 1 mg QD of trametinib observed by de Braud et al. support the initiation of our pivotal Phase 3 SEACRAFT-2 trial in NRASm melanoma. The higher response rates and prolonged PFS also further reinforce the advantage of this specific dosing regimen. We look forward to working with health authorities this year in order to support first patient dosing in SEACRAFT-2 during the first half of 2024."

Publication Highlights
Initial Evidence for the Efficacy of Naporafenib in Combination with Trametinib in NRAS-Mutant Melanoma: Results From the Expansion Arm of a Phase 1b, Open-Label Study
Dual blockade of the RAS/MAPK pathway has proven to be highly efficacious in patients with BRAF-mutant melanoma. However, similar dual blockade has not been approved in patients with NRASm melanoma. This Novartis-sponsored Phase 1b study evaluated the safety and preliminary efficacy of naporafenib plus trametinib at two recommended doses for expansion in patients with NRAS-mutant melanoma.

- Naporafenib plus trametinib demonstrated promising preliminary antitumor activity in heavily pretreated patients
- The safety profile of the combination was manageable with low discontinuation rates due to adverse events
- Naporafenib 200 mg BID + trametinib 1 mg QD vs. naporafenib 400 mg BID + trametinib 0.5 mg QD:
    - Confirmed objective response rate: 46.7% (7 of 15 patients) vs. 13.3% (2 of 15 patients)
    - Median duration of response: 3.75 months vs. 3.75 months
    - Median progression-free survival: 5.5 months vs. 4.2 months

About Naporafenib

Naporafenib (formerly LXH254) is a potent and selective pan-RAF inhibitor, with a potential first-in-class and best-in-class profile. Naporafenib has been dosed in over 500 patients to date, whereby safety, tolerability, pharmacokinetics, and pharmacodynamics have been established in both monotherapy and in certain combinations, with clinical proof-of-concept (PoC) data in combination with trametinib for NRAS-mutant (NRASm) melanoma, which includes NRAS Q61X melanoma, and preliminary clinical PoC data with trametinib for RAS Q61X in non-small cell lung cancer (NSCLC). Erasca plans to focus initially on advancing and securing regulatory approval for naporafenib plus trametinib in NRASm melanoma as part of the planned Phase 3 SEACRAFT-2 trial and in RAS Q61X tissue agnostic solid tumors as part of the planned Phase 1b SEACRAFT-1 trial, respectively. Erasca is also exploring additional combinations of naporafenib with other proprietary therapeutic agents in our pipeline.

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, including naporafenib; the planned advancement of our development pipeline, including the anticipated timing for the first patient dosing in the SEACRAFT-1 and SEACRAFT-2 trials, and other upcoming development milestones. 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; potential delays in the commencement, enrollment, and completion of clinical trials and preclinical studies; our dependence on third parties in connection with 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, including the clinical trial results discussed in this press release, not necessarily being predictive of future results; we have not conducted any clinical trials of naporafenib and are reliant on data generated by Novartis in prior clinical trials conducted by it; our planned SEACRAFT trials may not support the registration of naporafenib; the inability to realize any benefits from our current licenses, collaborations, and acquisitions and any future licenses, collaborations, or acquisitions, and our ability to fulfill our obligations under such arrangements; 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 marketable securities; our ability to maintain undisrupted business operations due to the COVID-19 pandemic and global geopolitical events, such as the ongoing conflict between Russia and Ukraine; unstable market and economic conditions and adverse developments with respect to financial institutions and associated liquidity risk may adversely affect our business, financial condition and stock price, and the broader economy and biotechnology industry; we may use our capital resources sooner than we expect; and other risks described in our prior filings with the Securities and Exchange Commission (SEC), including under the heading “Risk Factors” in our quarterly report on Form 10-K for the year ended December 31, 2022, 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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