Erasca Initiates SEACRAFT-2 Pivotal Phase 3 Trial Evaluating Naporafenib Plus Trametinib in Patients with NRAS-Mutant Melanoma

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Naporafenib is a potential first-in-class and best-in-class pan-RAF inhibitor for multiple RAS/MAPK pathway-driven tumors and has been dosed in over 500 patients to date

Favorable mOS and mPFS demonstrated in pooled analysis of Phase 1b and Phase 2 trials in NRASm melanoma

Randomized Stage 1 readout for naporafenib plus trametinib vs. trametinib monotherapy expected in 2025

SAN DIEGO, June 18, 2024 (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 initiation of the global SEACRAFT-2 Phase 3 trial evaluating the pan-RAF inhibitor naporafenib in combination with the MEK inhibitor trametinib (MEKINIST®) in patients with NRAS-mutant (NRASm) melanoma. Naporafenib is a potential first-in-class and best-in-class pan-RAF inhibitor that has been dosed in over 500 patients to date and is being developed to treat multiple types of RAS/MAPK pathway-driven tumors.

“NRASm melanoma is an aggressive disease with no approved targeted therapies, underscoring the high unmet need for these patients. We are pleased to announce the initiation of our SEACRAFT-2 pivotal Phase 3 trial, which has a two-stage design. Importantly, Stage 1 is expected to provide a randomized data readout of naporafenib plus trametinib against single agent trametinib in 2025 and will inform the randomized Phase 2 dose (RP2D) for the combination,” said Shannon R. Morris, M.D., Ph.D., Erasca’s chief medical officer. “Stage 2, which incorporates feedback from the United States Food and Drug Administration (FDA) and European health authorities, is designed for regulatory approval and will compare the combination against physician’s choice of chemotherapy or a single agent MEK inhibitor using dual primary endpoints of progression free survival (PFS) and overall survival (OS).”

A pooled analysis of the Phase 1b and Phase 2 trials of patients with NRASm melanoma dosed with naporafenib in combination with trametinib showed a median OS (mOS) of 13.0 and 14.1 months and a median PFS (mPFS) of 5.1 and 4.9 months at two doses of the combination, respectively. The pooled dataset at each dose compares favorably relative to historical benchmarks.

About SEACRAFT-2

SEACRAFT-2 is a randomized, pivotal Phase 3 trial evaluating the clinical efficacy of naporafenib in combination with trametinib (MEKINIST®) compared to physician’s choice of therapy (dacarbazine, temozolomide, or trametinib monotherapy) in the post-immunotherapy setting in patients with NRAS-mutant metastatic melanoma. A randomized Stage 1 readout for naporafenib plus trametinib compared to trametinib alone is expected in 2025.

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 select combinations. Clinical proof-of-concept (PoC) has been established for the combination with trametinib for patients with NRAS-mutant (NRASm) melanoma, which includes NRAS Q61X melanoma, and preliminary clinical PoC has been established for the combination with trametinib for patients with 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 SEACRAFT-2 pivotal Phase 3 trial and in RAS Q61X solid tumors as part of the ongoing SEACRAFT-1 Phase 1b trial, respectively. Erasca is also exploring additional combinations of naporafenib with other proprietary therapeutic agents in our pipeline. Naporafenib has received Fast Track Designation from the United States Food and Drug Administration (FDA) for patients with advanced NRASm melanoma.

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 one of 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 of the Stage 1 data readout for the SEACRAFT-2 trial, 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; the analysis of pooled Phase 1 and Phase 2 naporafenib plus trametinib data covers two clinical trials with different designs and inclusion criteria, which cannot be directly compared, and therefore may not be a reliable indicator of mOS data; due to differences between trial designs and subject characteristics, comparing data across different trials may not be a reliable indicator of data; 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; unfavorable results from preclinical studies or clinical trials; we have not completed 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; later developments with the FDA or EU health authorities may be inconsistent with the feedback received to date regarding our development plans and trial designs; our assumptions around which programs may have a higher probability of success may not be accurate, and we may expend our limited resources to pursue a particular product candidate and/or indication and fail to capitalize on product candidates or indications with greater development or commercial potential; 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; the inability to realize any benefits from our current licenses, collaborations, acquisitions, and collaborations, and any future licenses, acquisitions, or collaborations, and our ability to fulfill our obligations under such arrangements; our ability to obtain and maintain intellectual property protection for our product candidates; regulatory developments in the United States and foreign countries; Fast Track Designation may not lead to a faster development or regulatory review or approval process, and does not increase the likelihood that our product candidates will receive marketing approval; our ability to fund our operating plans with our current cash, cash equivalents, and marketable securities; and other risks described in our prior filings with the Securities and Exchange Commission (SEC), including under the heading “Risk Factors” in our annual report on Form 10-K for the year ended December 31, 2023, 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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