Erasca Granted FDA Fast Track Designation for Pan-RAF Inhibitor Naporafenib in Patients with Advanced NRAS-Mutated Melanoma

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First-in-class and best-in-class potential in NRAS-mutated melanoma and other RAS/MAPK pathway-altered solid tumors

Naporafenib has been dosed in more than 500 patients to date, establishing its safety, tolerability, and preliminary proof-of-concept in multiple indications

Pivotal Phase 3 SEACRAFT-2 trial initiation in NRAS-mutated melanoma on track for H1 2024

SAN DIEGO, Dec. 11, 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 that the United States Food and Drug Administration (FDA) has granted Fast Track Designation (FTD) to naporafenib in combination with trametinib (MEKINIST®) for the treatment of adult patients with unresectable or metastatic melanoma who have progressed on, or are intolerant to, an anti-programmed death-1 (ligand 1) (PD-(L)1)-based regimen, and whose tumors contain an NRAS mutation (NRASm). Naporafenib is an orally available, Phase 3-ready pan-RAF inhibitor with a potential first-in-class and best-in-class profile in NRASm melanoma and other RAS/MAPK pathway-altered solid tumors.

FTD is designed to help drugs reach patients faster by facilitating the development and expediting the review of drugs with the potential to fill an unmet medical need by treating a serious or life-threatening condition. Programs that receive FTD benefit from early and frequent interactions with the FDA during the clinical development process and, if relevant criteria are met, the FDA may consider reviewing portions of a marketing application before the sponsor submits the complete application.

“The outcomes for patients with NRASm melanoma after frontline immunotherapy (IO) treatment are dismal with low response rates and short median progression free survival (mPFS). By contrast, as previously presented by Novartis at the European Society for Medical Oncology (ESMO) Congress 2022 and as published in March 2023 by de Braud et al. in the *Journal of Clinical Oncology*, naporafenib in combination with trametinib has demonstrated strong and durable anti-tumor activity,” said Jonathan E. Lim, M.D., Erasca’s chairman, CEO, and co-founder. “We are now rapidly advancing clinical development of naporafenib in combination with trametinib in the post-IO setting in patients with NRASm melanoma with initiation of our pivotal Phase 3 SEACRAFT-2 trial expected in the first half of 2024. Receiving FTD further strengthens our ability to work closely with the FDA toward our goal of bringing this new therapy for difficult-to-treat melanoma to patients as soon as possible.”

NRASm melanoma comprises 20-30% of all melanomas and is associated with a worse prognosis compared to other alterations. Effective treatment options are needed for patients following progression on frontline IO with anti-CTLA-4 and/or anti-PD-(L)1 antibodies. Currently, chemotherapy is the approved post-IO standard of care with a 7% objective response rate (ORR) and 1.5 months mPFS (historical Phase 3 data generated when the drug was administered in the front-line/second-line setting). While not approved in this indication in the United States, the MEK inhibitor binimetinib is used off label and demonstrated a 15% ORR and 2.8 months mPFS (historical Phase 3 data generated when the drug was administered in the front-line/second-line setting). There are currently no approved therapies that target NRAS mutations. Erasca recently reported that End of Phase 2 meetings with the FDA and European health authorities confirmed the SEACRAFT-2 Phase 3 trial design and provided clarity on the registrational pathway.

About SEACRAFT-2

SEACRAFT-2 is a randomized, pivotal Phase 3 trial that will evaluate 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-mutated metastatic melanoma. Initiation of the SEACRAFT-2 trial is expected in H1 2024.

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 planned pivotal Phase 3 SEACRAFT-2 trial and in RAS Q61X tissue agnostic solid tumors as part of the Phase 1b SEACRAFT-1 trial, respectively. Erasca is also exploring additional combinations of naporafenib with other proprietary therapeutic agents in our pipeline. Naporafenib has received FDA Fast Track Designation 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 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: FTD may not result in a more expedited development or regulatory review process, and such a designation does not increase the likelihood that naporafenib in combination with trametinib will receive marketing approval in the United States; FTD does not change the standards for regulatory approval; the FDA may later decide that naporafenib in combination with trametinib no longer meets the conditions for FTD qualification or decide that the time period for FDA review or approval will not be shortened; our expectations regarding the potential therapeutic benefits of our product candidates and the potential patient populations for our product candidates, including naporafenib; our ability to realize the benefits from naporafenib receiving FTD from the FDA; and the planned advancement of our development pipeline, including the design of future trials and the anticipated timing of the data readout and dosing of the first patient in the SEACRAFT-1 and SEACRAFT-2 clinical trials, respectively. 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, data readouts, and completion of clinical trials and our preclinical studies; later developments with the FDA or European health authorities that may be inconsistent with the end of Phase 2 meetings, including that our planned SEACRAFT trials may not support the registration of naporafenib; 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 not necessarily being predictive of future results; preliminary results of a clinical trial are not necessarily indicative of final results and one or more of the clinical outcomes may materially change as patient enrollment continues, following more comprehensive reviews of the data and as more patient data become available; 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 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; regulatory developments in the United States and foreign countries; our dependence on third parties in connection with our existing collaboration and supply agreements; our ability to obtain and maintain intellectual property protection for our product candidates and maintain our rights under intellectual property licenses; the impact of global geopolitical events and war on our business; 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, 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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