Erasca Achieves Key Milestones for Naporafenib and ERAS-801 Programs and Extends Cash Runway

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Gained alignment with global health authorities for pivotal Phase 3 SEACRAFT-2 trial design for naporafenib plus trametinib in NRAS mutant melanoma; initiation on track for H1 2024

Completed dose escalation and identified MTD for ERAS-801, supporting enrollment of expansion cohorts in recurrent GBM

Extended cash runway to H1 2026 following strategic prioritization of programs

SAN DIEGO, Nov. 28, 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 program updates for pan-RAF inhibitor naporafenib and central nervous system (CNS)-penetrant EGFR inhibitor ERAS-801, as well as a strategic program prioritization that extends its projected cash runway from H2 2025 to H1 2026.

“We are excited about the recent progress across key clinical programs, including the regulatory alignment with U.S. and European health authorities for our global naporafenib registrational trial which is on track to initiate in the first half of 2024, the establishment of the maximum tolerated dose (MTD) for ERAS-801 in patients with glioblastoma (GBM), and the promising preliminary activity of ERAS-007 plus encorafenib and cetuximab (EC) in EC-naïve patients with BRAF mutant colorectal cancer (CRC) presented at ASCO,” said Jonathan E. Lim, M.D., Erasca’s chairman, CEO, and co-founder. “To further maximize resources, we have strategically refined our pipeline to focus on programs with the greatest therapeutic potential for patients with high unmet needs using a data-driven approach. As such, we are deprioritizing our ERAS-601 clinical trial (FLAGSHP-1) and our preclinical ERAS-5 ULK inhibitor and ERAS-10 protein degrader programs. Importantly, this pipeline prioritization extends our cash runway into the first half of 2026 and through key milestones, including important clinical trial readouts for naporafenib, ERAS-801, and ERAS-007.”

Recent Program Updates

Naporafenib Plus Trametinib for Patients with NRAS mutant (NRASm) Melanoma in Pivotal SEACRAFT-2 Trial
End of Phase 2 meetings with U.S. Food and Drug Administration (FDA) and European health authorities confirm SEACRAFT-2 Phase 3 trial design and provide clarity on registrational pathway:

- Enrollment of patients with high unmet medical need who progressed on, or are intolerant to, standard of care immune checkpoint inhibitor therapy
- Comparator arm is physicians’ choice of cytotoxic chemotherapy or trametinib
- Dual primary endpoint evaluation of progression free survival (PFS) and overall survival (OS), with PFS acceptable for potential initial approval
- The Phase 3 trial consists of two stages: a randomized, controlled, dose optimization stage, for which we expect to have a data readout in 2025, and a randomized, controlled stage to support regulatory approval
- *Phase 3 SEACRAFT-2 trial initiation remains on track for H1 2024*

ERAS-801 for Patients with Recurrent GBM in Phase 1 THUNDERBBOLT-1 Trial
Thirty-three patients with recurrent glioblastoma (rGBM) were enrolled in seven dose escalation cohorts. ERAS-801 monotherapy has been granted Orphan Drug and Fast Track Designations (ODD and FTD) by the FDA. Interest in THUNDERBBOLT-1 from trial investigators continues to be robust.

- MTD identified as 240 mg once a day (QD) and MTD-1 identified as 160 mg QD for ERAS-801
- ERAS-801 was safe and tolerable at the MTD and MTD-1 dose levels. The adverse event profile was consistent with the mechanism of action and observations in non-clinical studies
- ERAS-801 exhibited well behaved pharmacokinetic (PK) characteristics: ERAS-801 showed rapid absorption and had dose-dependent increases in PK exposure. Steady-state PK exposures at doses of 160 mg QD and above exceeded the concentration at which 90% tumor growth inhibition was achieved in the GBM patient-derived orthotopic xenograft (PDOX) mouse model.
- Expansion cohorts actively enrolling to collect additional safety, tolerability, and preliminary efficacy data to support dose optimization and selection
- *Phase 1 dose escalation data to be presented at a scientific meeting in H1 2024; expansion cohort data are anticipated in H2 2024*

Shannon R. Morris, M.D., Ph.D., Erasca’s chief medical officer, added, “ERAS-801 is an orally bioavailable CNS-penetrant EGFR inhibitor specifically designed to target the unique EGFR alterations observed in GBM, initially as a monotherapy treatment. Identification of the MTD signals the transition of ERAS-801 to the next stage of development with a focus on characterizing the clinical activity of the molecule in patients with EGFR-amplified rGBM, who may achieve maximum benefit from treatment. Notably, this population represents nearly half of all patients with GBM and 85% of all patients with EGFR-altered GBM.”

Prioritized Clinical Programs and Key Upcoming Milestones
Naporafenib – Pan-RAF Inhibitor

- Dosing of the first patient in pivotal Phase 3 SEACRAFT-2 trial in patients with NRASm melanoma expected H1 2024
- Initial signal-seeking Phase 1b efficacy data in relevant tumor types from patients with RAS Q61X solid tumors in ongoing SEACRAFT-1 trial expected between Q2-Q4 2024

ERAS-801 – CNS-penetrant EGFR Inhibitor

- Phase 1 monotherapy dose escalation and expansion data in rGBM expected in 2024

ERAS-007 – ERK1/2 Inhibitor

- Initial dose expansion data from Phase 1b/2 HERKULES-3 trial further evaluating encouraging early efficacy data with ERAS-007 in combination with EC in EC-naïve patients with BRAF mutant CRC expected between H2 2023 and H1 2024

Deprioritized Opportunities
Select trials or programs were deprioritized, despite their potential differentiation, to focus the company's resources on the most promising programs, which is expected to extend the company's cash runway from H2 2025 to H1 2026:

- **FLAGSHP-1 –** Phase 1b combination trial of ERAS-601 SHP2 inhibitor with cetuximab was deprioritized. Though ERAS-601 achieved confirmed responses as a monotherapy and in combination with cetuximab, preliminary data do not justify further development of this combination in FLAGSHP-1 indications
- **ERAS-5 –** Preclinical ULK inhibitor
- **ERAS-10 –** Preclinical protein degrader

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 ability to execute on the upcoming near-term catalysts for our clinical programs; our expectations regarding the potential therapeutic benefits and safety profile of our product candidates, including naporafenib, ERAS-007, and ERAS-801; the planned advancement of our development pipeline, including the design of future trials and anticipated timing of the first patient dosing in the SEACRAFT-2 trial, the anticipated timing of data readouts for the SEACRAFT-1, HERKULES-3, and THUNDERBBOLT-1 trials, and other upcoming development milestones; our ability to realize the benefits from ERAS-801 receiving ODD and FTD from the FDA; and our expectation that our current cash, cash equivalents, and marketable securities will fund our operations into the first half of 2026. 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 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 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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