Erasca Announces Strong Momentum for Naporafenib and RAS Targeting Franchise

10.24.2024

Positive preliminary Phase 1b SEACRAFT-1 data for naporafenib plus trametinib reinforce therapeutic potential in NRASm melanoma and further support ongoing Phase 3 SEACRAFT-2 trial

SEACRAFT-2 has potential for approval based on alignment with US and European regulatory agencies on path for tissue-specific indication in melanoma; Stage 1 randomized data expected in 2025

Rapid progress across RAS targeting franchise; planned IND submissions remain on track

Erasca to host investor event today at 8:30 AM Eastern Time

SAN DIEGO, Oct. 24, 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 clinical progress for naporafenib and preclinical execution across the company's RAS targeting franchise.

"The SEACRAFT-1 trial in patients with RAS Q61X solid tumors has successfully accomplished several key objectives: delivering clinical data supporting the potential for durable efficacy in patients with NRAS-mutant (NRASm) melanoma, who currently have limited treatment options following frontline immunotherapy; identifying the most promising antitumor signal for the combination, which has been observed in melanoma patients, supporting a tissue-specific approach; and reducing the frequency and severity of dermatologic toxicities through mandatory primary prophylaxis," said Shannon R. Morris, M.D., Ph.D., Erasca's chief medical officer. "In totality, these data strengthen our conviction in the ongoing SEACRAFT-2 Phase 3 trial, for which we gained US and European alignment on the regulatory path in patients with NRASm melanoma. We look forward to randomized dose optimization data from Stage 1 of this trial, which is expected in 2025."

Jonathan E. Lim, M.D., Erasca's chairman, CEO, and co-founder, added, "We were excited to bolster our pipeline with the in-licensing of our RAS-targeting franchise in May, including the pan-RAS molecular glue ERAS-0015 and the pan-KRAS inhibitor ERAS-4001. These two assets with competitive profiles, potential for significant patient benefit, and broad application across solid tumors, have become key priorities for the company. In addition to reproducing data in-house supporting the best-in-class potential of both compounds, we continue to execute effectively and efficiently across several functional disciplines, including generating additional in vivo data and progressing the in-life portion of the Good Laboratory Practice (GLP) toxicology studies as anticipated, as well as advancing our drug substance and drug product development and manufacturing activities for both molecules according to plan. Investigational new drug (IND) application submissions remain on track for the first quarter of 2025 for ERAS-4001 and the first half of 2025 for ERAS-0015."

Naporafenib Program Update

Naporafenib is a potential first-in-class and best-in-class pan-RAF inhibitor. Naporafenib plus trametinib (MEKINIST®) is being evaluated in the Phase 1b SEACRAFT-1 trial in patients with RAS Q61X mutations and the Phase 3 SEACRAFT-2 trial in patients with NRASm melanoma. In a post-hoc pooled analysis of Phase 1b and Phase 2 data from trials in patients with NRASm melanoma conducted by Novartis, naporafenib in combination with trametinib demonstrated favorable median overall survival (mOS) and median progression free survival (mPFS). The U.S. Food and Drug Administration has granted Fast Track Designation to naporafenib plus trametinib for the treatment of NRASm melanoma.

- **NRASm melanoma has a high unmet medical need**
  - 25-30% of melanomas are NRASm, which has a worse prognosis vs. other molecular alterations
  - Current treatment options following frontline immunotherapy are poor: chemotherapy (approved standard of care) demonstrated 7% ORR and 1.5 months mPFS; binimetinib demonstrated 15% ORR and 2.8 months mPFS
- **Promising initial Phase 1b efficacy results in the SEACRAFT-1 melanoma cohort further bolsters rationale for pursuing NRASm melanoma indication*:**
  - 40% (4/10) response rate observed in the melanoma cohort, including three confirmed partial responses (cPR) and one unconfirmed partial response (uPR); the melanoma cohort in SEACRAFT-1 is representative of the patient population currently being enrolled in the pivotal SEACRAFT-2 trial
  - 70% (7/10) of patients were on treatment as of the data cutoff, including all four responders
- **Generally well-tolerated with mostly low-grade adverse events in the majority of patients***
  - Results suggest that mandatory primary rash prophylaxis helped reduce frequency and severity of dermatological toxicities, reduced drug discontinuation rate due to adverse events, and improved the tolerability profile as measured by an increased relative dose intensity as compared to the prior clinical trials of naporafenib plus trametinib conducted by Novartis, which did not include the use of mandatory primary rash prophylaxis
- **Data reinforce potential of ongoing Phase 3 SEACRAFT-2 trial in patients with NRASm melanoma**
  - Potential for approval in both US and Europe based on high unmet need and regulatory alignment
  - Randomized dose optimization data from Stage 1 of the SEACRAFT-2 Phase 3 trial expected in 2025

* Safety data cutoff date was September 3, 2024. Efficacy data cutoff date was September 5, 2024

RAS Targeting Franchise Update (ERAS-0015 and ERAS-4001)

ERAS-0015 is a preclinical pan-RAS molecular glue with best-in-class potential for patients with RASm solid tumors that showed up to 10-fold greater potency and favorable absorption, distribution, metabolism, and excretion (ADME) properties and pharmacokinetics (PK) performance in preclinical studies when compared to another pan-RAS molecular glue currently in clinical development. ERAS-4001 is a preclinical pan-KRAS inhibitor that has shown first-in-class and best-in-class potential with high potency, strong antitumor activity, favorable ADME and PK properties in preclinical studies, including oral bioavailability, and ability to spare H/NRAS while limiting resistance through KRAS wild type activation.

- Nonclinical data continue to support potential best-in-class profiles, including data generated in-house
- In-life portion of Good Laboratory Practice (GLP) toxicology studies tracking as anticipated: ERAS-0015 completed, ERAS-4001 near completion
- On track to achieve previously articulated guidance of IND filing in H1 2025 for ERAS-0015 and Q1 2025 for ERAS-4001

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 pipelines 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, ERAS-0015, and ERAS-4001; the planned advancement of our development pipeline, including the anticipated timing of the data readout for Stage 1 of the SEACRAFT-2 trial, our alignment with regulatory authorities on the regulatory pathway for naporafenib, and the anticipated timing of the IND filings for ERAS-0015 and ERAS-4001. 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; preliminary results of clinical trials 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 more patient data become available; 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 survival data; due to differences between trial designs and subject characteristics, comparing data across different trials may not be a reliable indicator of data; our assumptions about ERAS-0015's and ERAS-4001's development potential are based in part on the preclinical data generated by the licensors and we may observe materially and adversely different results as we conduct our planned studies and trials; results from preclinical studies or early clinical trials not necessarily being predictive of future results; we only have one product candidate in clinical development and all of our other development efforts are in the preclinical or development stage; our SEACRAFT trials may not support the registration of naporafenib; 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, data readout, 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; the inability to realize any benefits from our current licenses, acquisitions, and collaborations, and any future licenses, acquisitions, or collaborations, and our ability to fulfill our obligations under such arrangements; regulatory developments in the United States and foreign countries; 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; 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 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; 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.

Contact:
Joyce Allaire
LifeSci Advisors, LLC
jallaire@lifesciadvisors.com

Source: Erasca, Inc.

ERASCA™

Source: Erasca, Inc.