Erasca Provides Update on Clinical Program for ERK Inhibitor ERAS-007 and Refines Pipeline

June 5, 2023

ERAS-007 100 mg BID-QW + encorafenib + cetuximab (EC) in EC-naïve patients with BRAFm CRC showed a 50% (3/6) response rate (2 cPR, 1 uPR), reinforcing ERAS-007 as a potential best-in-class ERK inhibitor

Ongoing clinical programs for naporafenib, ERAS-007, ERAS-601, and ERAS-801 in patients with RAS/MAPK pathway-driven tumors continue to offer potential differentiation and near-term catalysts

Strategic pipeline prioritization sharpens focus on existing programs with encouraging signals of activity

Erasca to host investor event today at 4:30 PM Eastern Time

SAN DIEGO, June 05, 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 promising preliminary Phase 1b data for ERK inhibitor ERAS-007 in patients with metastatic BRAF V600E-mutated (BRAFm) colorectal cancer (CRC) and provided a portfolio update. Erasca will host a virtual investor event to discuss these updates today at 4:30 PM ET. To register for the event, please click here.

“We are pleased that the early ERAS-007 clinical data continue to reinforce its potential to become a backbone for combination therapy,” said Jonathan E. Lim, M.D., Erasca’s chairman, CEO, and co-founder. “Moreover, through our signal-seeking trials, we have tested three biological hypotheses: preventing in-pathway resistance, reversing in-pathway resistance, and targeting adjacent pathways. We believe the encouraging efficacy data for ERAS-007 in combination with encorafenib and cetuximab in EC-naïve patients with BRAFm CRC (preventing in-pathway resistance) provide compelling evidence to continue with further enrollment in this patient population.”

Dr. Lim continued, “Due to a lack of clinical activity, we will not continue exploring ERAS-007 combined with palbociclib in patients with RAS-mutated gastrointestinal malignancies (targeting adjacent pathways) or ERAS-007 combined with osimertinib in patients with post-osimertinib EGFR-mutated non-small cell lung cancer (reversing in-pathway resistance). We have also decided to deprioritize certain discovery programs: ERAS-9 (SOS1), ERAS-11 (MYC), and ERAS-2/3 (RAS switch-II groove targeting), but are pursuing other promising research approaches to target RAS mutations beyond G12C. Further refining our efforts and prioritizing resources will allow us to focus on clinical and research programs with potential therapeutic differentiation and will increase our capacity to realize the many exciting opportunities ahead of us to help patients. We continue to be well positioned to execute on important catalysts over the next 18 months and beyond for our four clinical programs, our pan-RAF inhibitor naporafenib, ERK inhibitor ERAS-007, SHP2 inhibitor ERAS-601, and CNS-penetrant EGFR inhibitor ERAS-801.”

ERAS-007 Development Update
Meaningful activity in patients with EC-naïve BRAFm CRC supports initial focus on and dose expansion of this patient population*:

- 50% (3/6) response rate, including two confirmed partial responses (cPR) and one unconfirmed partial response (uPR), and 67% (4/6) disease control rate (DCR; defined as complete response + partial response + stable disease) in EC-naïve response evaluable patients at the highest dose of ERAS-007 tested (100 mg BID-QW), with duration of exposure for both cPRs >40 weeks as of the data cutoff date; across all dose levels in EC-naïve response evaluable patients, 38% (3/8) response rate, including two cPRs and one uPR, and 63% (5/8) DCR. Per site communication, the patient with the uPR was still in response at the subsequent scan (May 26, 2023), which was conducted 25 days after the first post-baseline scan
- ERAS-007 + EC was generally well tolerated with mostly low-grade treatment-related adverse events (TRAEs) at all combination doses tested. No Grade 4 or 5 TRAEs were observed
- One dose-limiting toxicity (DLT) was reported for ERAS-007 100 mg BID-QW + EC (Grade 3 macular edema)
- Pharmacokinetic (PK) exposures of ERAS-007, encorafenib, and cetuximab were comparable to the respective monotherapy PK data, suggesting no apparent PK drug-drug interactions (DDI) between the study drugs

* Safety data cutoff date was March 23, 2023. Efficacy data cutoff date was May 21, 2023

Across the HERKULES studies, early clinical data reinforce ERAS-007’s potential to be a backbone for combination therapy:

- Target PK profile achieved with adequate exposures and well-defined PK in monotherapy and combinations
- No apparent PK DDI liabilities were observed for ERAS-007 when dosed in combination with multiple approved therapies
- ERAS-007 has been safely combined with other agents at biologically relevant doses and schedules
- ERAS-007 monotherapy responses observed in multiple tumor types support further evaluation of intermittent scheduling in combination
- Encouraging signs of efficacy for select ERAS-007 combinations

Portfolio Update

A data-driven prioritization focuses Erasca's resources on opportunities with the highest probability of success for patients.

Development Programs

- **HERKULES-3: ERAS-007 + EC in EC-naïve patients with BRAFm CRC (preventing in-pathway resistance):** Conducting dose expansion based on encouraging early efficacy data in EC-naïve patients
- **HERKULES-3: ERAS-007 + EC in EC-treated patients with BRAFm CRC (reversing in-pathway resistance):** Gating evaluation on efficacy data in EC-naïve CRC population (i.e., EC-treated population may be explored if efficacy data continue to be promising in the EC-naïve population), as it is more challenging to show treatment benefit in EC-treated population than in EC-naïve population
- **HERKULES-2: ERAS-007 + osimertinib in patients with post-osimertinib EGFR-mutant NSCLC (reversing in-pathway resistance):** Deprioritized as clinical efficacy data do not support continued evaluation
- **HERKULES-3: ERAS-007 + palbociclib in patients with KRAS- or NRAS-mutant CRC and KRAS-mutant PDAC (targeting adjacent pathways):** Deprioritized as clinical efficacy data do not support continued evaluation
- **HERKULES-1: ERAS-007 + ERAS-601 in patients with advanced solid tumors:** Deprioritized as dose escalation safety data do not support continued evaluation of regimen tested
- **AURORAS-1: ERAS-3490 in patients with KRAS G12C-mutated solid tumors:** Deprioritized due to increasingly competitive landscape for small- and mid-cap biopharma companies despite the program's potential differentiation

Research Programs

- **ERAS-9 SOS1:** Deprioritized to focus on SHP2 as the key upstream RAS/MAPK pathway node due to promise of ERAS-601 SHP2 inhibitor
- **ERAS-11 MYC:** Deprioritized as preclinical characterization does not support continued work
- **ERAS-2/3 RAS Switch-II Groove targeting:** Deprioritized and pursuing other promising research approaches to target RAS mutations beyond G12C

Key Upcoming Milestones
Erasca re-affirmed its prior guidance for the following, with respect to anticipated key milestones and clinical trial readouts:

- **Naporafenib (pan-RAF inhibitor)**
  - **SEACRAFT-1:** Phase 1b trial for naporafenib plus trametinib in patients with RAS Q61X solid tumors
    - First patient dosing expected in second half of 2023
    - Initial Phase 1b combination signal-seeking efficacy data in relevant tumor types expected between the second and fourth quarters of 2024
  - **SEACRAFT-2:** Randomized pivotal Phase 3 trial for naporafenib plus trametinib in patients with NRASm melanoma
    - First patient dosing expected in first half of 2024
- **ERAS-007 (ERK1/2 inhibitor)**
  - **HERKULES-3:** Phase 1b trial for ERAS-007 plus EC in EC-naïve BRAFm CRC patients
    - Phase 1b combination expansion data in patients with BRAFm CRC expected between the second half of 2023 and the first half of 2024
- **ERAS-601 (SHP2 inhibitor)**
  - **FLAGSHP-1:** Phase 1b trial in patients with advanced solid tumors
    - Phase 1b combination expansion data in relevant patient populations, including patients with human papillomavirus (HPV)-negative advanced head and neck squamous cell carcinoma (HNSCC) expected in first half of 2024
- **ERAS-801 (CNS-penetrant EGFR inhibitor)**
  - **THUNDERBBOLT-1:** Phase 1 trial in patients with recurrent glioblastoma (GBM)
    - Initial Phase 1 monotherapy dose escalation data in patients with recurrent GBM expected in second half of 2023

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 important catalysts over the next 18 months and beyond for our four clinical programs; our expectations regarding the potential therapeutic benefits and safety profile of our product candidates, including naporafenib, ERAS-007, ERAS-601, and ERAS-801; and the planned advancement of our development pipeline, including the anticipated timing of the first patient dosing in the SEACRAFT series of trials, the anticipated timing of data readouts for the

SEACRAFT-1, HERKULES-3, FLAGSHP-1, and THUNDERBBOLT-1 trials, and other upcoming development milestones, and the planned deprioritization of certain programs. 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: 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 becomes available, including the risk that an uPR to treatment may not ultimately result in a cPR to treatment after follow-up evaluations; 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 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; 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; 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 ending 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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Source: Erasca, Inc.

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