Erasca Presents Compelling Preclinical Data Supporting Clinical Development of Potentially Best-In-Class Programs ERAS-007, ERAS-601, and ERAS-3490 at 2022 AACR Annual Meeting

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ERAS-007 is a potent and selective small molecule ERK1/2 inhibitor with long target residence time, which promotes sustained RAS/MAPK pathway inhibition

ERAS-601 is a potent and selective small molecule SHP2 inhibitor with broad anti-tumor activity that blocks oncogenic signal transduction to multiple pathways to delay the onset of therapeutic resistance

ERAS-3490 is a CNS-penetrant KRAS G12C inhibitor with robust systemic and CNS activity in development for the treatment of KRAS G12C mutant lung adenocarcinoma

SAN DIEGO, April 12, 2022 (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 preclinical data from six poster presentations at the American Association for Cancer Research (AACR) Annual Meeting in New Orleans, Louisiana. The posters are available online at Erasca.com/science/#presentations.

"To shut down the highly oncogenic RAS/MAPK pathway, we are targeting multiple nodes and cooperative mechanisms using a data-driven clinical development effort that identifies single agent and combinations with potential to significantly prolong survival in patient populations with high unmet needs," said Jonathan E. Lim, M.D., Erasca's chairman, CEO, and co-founder. "This year, we were pleased to present six posters at the AACR annual meeting highlighting preclinical data supporting the clinical development of three of our best-in-class programs, including our ERK1/2 inhibitor ERAS-007, our SHP2 inhibitor ERAS-601, and one of our CNS-penetrant KRAS G12C inhibitors ERAS-3490, as well as our choice of combination partners for these product candidates."

Poster Presentation Highlights

Abstract 2672: ERAS-007 is a selective ERK1/2 inhibitor with preclinical activity across RAS/MAPK pathway-driven CRC models

ERAS-007 demonstrates promising preclinical activity across a wide range of RAS/MAPK pathway-driven CRC models as a monotherapy and in combination. Over 50% of patients with colorectal cancer (CRC) have activating mutations in the RAS/MAPK signaling pathway, with available targeted therapies demonstrating limited overall response rates and duration of response.

- ERAS-007 is a highly potent and selective small molecule ERK1/2 inhibitor with long target residence time that promotes sustained RAS/MAPK pathway inhibition
- ERAS-007 demonstrates promising preclinical activity across a wide range of RAS/MAPK pathway-driven CRC models both as a monotherapy and in combination
- ERAS-007 + encorafenib and cetuximab in BRAF V600E CRC, and ERAS-007 + palbociclib in KRAS/NRAS mutant CRC are currently being evaluated in the HERKULES-3 Phase 1b/2 master protocol clinical trial in patients with advanced gastrointestinal malignancies (NCT05039177), with initial data expected between the fourth quarter of 2022 and the first half of 2023

Abstract 2671: ERAS-601, a potent allosteric inhibitor of SHP2, demonstrates compelling single agent anti-tumor activity in RAS/MAPK-driven tumor models

ERAS-601 blocks growth signals from multiple receptor tyrosine kinases (RTKs) to help prevent cancer growth. SHP2 acts as a convergent node for RTK signaling, relaying growth and survival signals from RTKs to intracellular signaling pathways. ERAS-601 inhibits SHP2, blocking oncogenic signal transduction through SHP2, which helps delay development of therapeutic resistance.

- ERAS-601 inhibits loading of RAS-GTP and demonstrates anti-proliferative activity in KRAS mutant, BRAF Class III, NF1 loss of function (LOF), and EGFR-activated cell lines
- ERAS-601 achieves substantial systemic exposure and inhibits tumor growth in multiple RAS/MAPK-activated CDX and PDX models harboring EGFR, KRAS, BRAF Class III, and NF1 LOF mutations
- ERAS-601 is being investigated in the ongoing FLAGSHP-1 Phase 1/1b trial in patients with advanced solid tumors (NCT04670679), with initial data expected in the second half of 2022

Abstract 2670: ERAS-601, a potent allosteric inhibitor of SHP2, synergistically enhances the efficacy of sotorasib/adagrasib and cetuximab in NSCLC, CRC, and HNSCC tumor models

ERAS-601 can serve as a backbone of combination therapy to enhance efficacy of other targeted therapies. Treatment durability with KRAS G12C inhibitors in non-small cell lung cancer (NSCLC) and with EGFR antibodies in CRC is limited due to RAS and RTK reactivation. ERAS-601 + sotorasib/adagrasib and ERAS-601 + cetuximab were evaluated for enhanced efficacy or prevention of resistance in advanced solid tumor models.

- ERAS-601 + KRAS G12C inhibitors synergistically inhibits cell viability in KRAS G12C cells and achieves tumor inhibition superior to either agent alone in KRAS G12C NSCLC and CRC CDX and PDX models

- ERAS-601 + cetuximab enhances anti-proliferative activity and achieves tumor growth inhibition superior to respective monotherapies in RAS/RAF wildtype HPV-negative head and neck squamous cell carcinomas (HNSCC) and triple wildtype (KRAS/NRAS/BRAF wildtype) CRC CDX and PDX models
- ERAS-601 + sotorasib is being investigated in the ongoing HERKULES-2 Phase 1b/2 master protocol in patients with advanced NSCLC (NCT04959981)
- ERAS-601 + cetuximab is being investigated in the FLAGSHP-1 Phase 1/1b trial in patients with advanced solid tumors, including RAS/RAF wildtype CRC and HPV-negative HNSCC tumors (NCT04670679), with initial data expected between the fourth quarter of 2022 and the first half of 2023

Abstract 3345: ERAS-601, a potent allosteric inhibitor of SHP2, synergistically enhances the activity of a FLT3 inhibitor, gilteritinib, in FLT3-mutated AML tumor models

ERAS-601 works synergistically with gilteritinib to inhibit RAS/MAPK signaling and cell viability of FLT3-mutated acute myeloid leukemia (AML), achieving more durable tumor inhibition than either agent alone. AML is dependent on RAS/MAPK pathway signaling, with prevalent mutations across multiple nodes of this pathway. Gilteritinib, a FLT3 inhibitor, has demonstrated clinical activity, but resistance limits the benefit of gilteritinib monotherapy. ERAS-601 + gilteritinib was evaluated non-clinically in FLT3-mutated AML models to assess potential for improvement with co-suppression of the RAS/MAPK pathway.

- ERAS-601 + gilteritinib inhibits oncogenic RAS/MAPK pathway signaling as measured by ERK1/2 phosphorylation and synergistically inhibits cellular viability of FLT3-mutated AML cells *in vitro*
- ERAS-601 + gilteritinib achieves more durable tumor growth inhibition *in* vivo than either agent alone in multiple FLT3-ITD mutant models
- ERAS-601 + gilteritinib in FLT3-altered AML is being investigated in the HERKULES-4 Phase 1b/2 master protocol trial in patients with hematologic malignancies (NCT05279859)

Abstract 2669: ERAS-007 (ERK1/2 inhibitor) + ERAS-601 (SHP2 inhibitor) exhibit nonclinical combination activity across KRAS mutated NSCLC, CRC, and PDAC tumor models

Erasca's first MAPKlamp, ERAS-007 + ERAS-601, demonstrates combination activity in KRAS mutant tumor models by inhibiting both an upstream node of the RAS/MAPK pathway, SHP2, and the most distal node, ERK1/2. KRAS mutations occur in approximately 25% of all cancers and promote oncogenesis via constitutive activation of the RAS/MAPK pathway. Rapid emergence of resistance, often mediated by reactivation of RAS/MAPK signaling, limits monotherapy activity. Erasca's first MAPKlamp (ERAS-007 + ERAS-601) was evaluated for the potential to prevent RAS/MAPK pathway reactivation more robustly than inhibition of a single node alone.

- The ERAS-007 + ERAS-601 MAPKlamp combination inhibits colony growth more potently than either agent alone in KRAS mutant NSCLC, CRC, and PDAC cell lines *in vitro*
- The ERAS-007 + ERAS-601 MAPKlamp combination achieved superior tumor growth inhibition and regression over either agent alone in KRAS mutant NSCLC, CRC, and PDAC xenografts *in vivo*
- These data support the clinical development of the ERAS-007 + ERAS-601 MAPKlamp combination

Abstract 2675: Discovery of potent CNS-penetrant covalent KRAS G12C inhibitors

Erasca has discovered multiple central nervous system (CNS)-penetrant KRAS G12C inhibitors (ERAS G12Ci's) with robust systemic and CNS activity, highlighting these inhibitors' potential to address systemic cancers with CNS involvement. The KRAS G12C mutation occurs in 14% of lung adenocarcinoma tumors, with brain metastases in up to 40% of patients. ERAS-3490, an ERAS G12Ci, is designed to address the high prevalence of CNS metastases in KRAS G12C mutant lung cancer.

- ERAS G12Ci's achieve 11-68% brain/plasma concentration ratios in intravenously infused rats, with brain concentrations between 91-290 ng/g, and potently inhibit cell proliferation and RAS/MAPK signaling in KRAS G12C cell lines
- ERAS-3490 has robust anti-tumor activity in KRAS G12C mutant MIA PaCa-2, NCI-H1373, and NCI-H2122 CDX subcutaneous models
- ERAS-3490 shows robust anti-tumor activity and dose-dependent survival benefit in the KRAS G12C NSCLC intracranial model NCI-H1373-luc, a nonclinical model of NSCLC CNS metastasis
- IND filing for ERAS-3490 in KRAS G12C mutant NSCLC is expected in the second half of 2022

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 expectations regarding the potential therapeutic benefits of our product candidates, including ERAS-007, ERAS-601, and ERAS-3490; the planned advancement of our development pipeline, including the anticipated timing of data readouts for our clinical trials, the expected timing of the IND filing for ERAS-3490, 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; 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; the inability to realize any benefits from our current licenses and acquisitions 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; 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 investments; our ability to maintain undisrupted business operations due to the COVID-19 pandemic, including delaying or disrupting our clinical trials, manufacturing, and supply chain; 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, 2021, 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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