Erasca Presents New Preclinical Data Reinforcing Best-in-Class Potential of RAS-Targeting Franchise at the 2025 AACR Annual Meeting

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ERAS-0015 and ERAS-4001 showed robust anti-tumor activity as monotherapy and combination therapy

First-in-class examples of direct SHOC2 binders and modulators of SMP complex assembly identified with potential to block oncogenic RAS/MAPK pathway signaling

SAN DIEGO, April 29, 2025 (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 presented new preclinical data reinforcing the best-in-class profiles of Erasca's RAS-targeting franchise at the American Association for Cancer Research (AACR) Annual Meeting in Chicago, Illinois. The Company also presented potential first-in-class examples of direct SHOC2 binders and modulators of SMP complex assembly, representing a new approach to block oncogenic RAS/MAPK pathway signaling. The posters are available online at Erasca.com/science/#presentations.

"We were pleased to present new preclinical data at this year's AACR meeting further solidifying our understanding of the properties that support the best-in-class potential of our pan-RAS molecular glue ERAS-0015 and the best-in-class/first-in-class potential of our pan-KRAS inhibitor ERAS-4001. We also showcased our research capabilities with, to our knowledge, the first identification of direct SHOC2 binders targeting the RAS/MAPK pathway in collaboration with our scientific advisory board member Pablo Rodriguez-Viciana," said Jonathan E. Lim, M.D., Erasca's chairman, CEO, and co-founder. "Importantly, these data reinforce the favorable pharmacokinetic properties that allow for robust anti-tumor activity at significantly lower doses of ERAS-0015 versus the leading pan-RAS molecular glue in development, as well as the potential expanded therapeutic index of ERAS-4001 through selective targeting of key KRAS mutations. We are excited to achieve our goal of advancing development of both RAS-targeting compounds in the clinic this year."

Poster Presentation Highlights

Abstract 390 – ERAS-0015 is a pan-RAS molecular glue with best-in-class potential in RAS mutant solid tumors

ERAS-0015 demonstrated favorable pharmacokinetic properties including longer residence time and greater tissue exposure that led to robust anti-tumor activity alone and in combination at doses lower than the leading pan-RAS molecular glue in development. ERAS-0015 is a pan-RAS molecular glue designed to shut down pathogenic signaling mediated by mutant and wildtype RAS by targeting RAS in the GTP-bound state.

- 8-21-fold greater cyclophilin A (CypA) binding for ERAS-0015 vs. pan-RAS molecular glue comparator RMC-6236
- ERAS-0015 dose-dependently formed a ternary complex with active state RAS and CypA, which blocks formation of additional downstream effector complexes
- Potent inhibition of proliferation with ERAS-0015 across a panel of cell lines spanning diverse tumor tissues and RAS mutations
- Preferential drug distribution into tumor tissues
- Promising monotherapy and combination activity across multiple RAS mutant models

Abstract 4367 – ERAS-4001 is a pan-KRAS inhibitor with robust anti-tumor activity in KRAS altered solid tumors

ERAS-4001 potentially has an expanded therapeutic index relative to pan-RAS inhibitors by selectively targeting both mutant and wildtype KRAS, leading to significant tumor growth inhibition alone and in combination. Selectively targeting both wildtype (WT) and oncogenic KRAS may address resistance mechanisms to mutant-selective KRAS inhibitors that are driven by WT KRAS activity. A potential first-in-class pan-KRAS inhibitor, ERAS-4001 is a novel, highly potent pan-KRAS inhibitor that blocks mutant and WT KRAS, potentially offering improved tolerability relative to pan-RAS inhibitors by sparing NRAS and HRAS.

- ERAS-4001 selectively inhibited KRAS mutant enzymes and WT KRAS over WT HRAS and NRAS
- ERAS-4001 inhibited 3D cell viability and proliferation in 13 G12X mutant and one wildtype KRAS amplified cell lines across indications with single digit nanomolar IC50s
- Dose-dependent tumor growth inhibition and significant antitumor efficacy with ERAS-4001 monotherapy in KRAS mutant xenograft models
- Robust tumor growth inhibition with ERAS-4001 plus anti-PD-1 or cetuximab in KRAS mutant models
- Promising antitumor monotherapy and combination activity across multiple KRAS mutant models

Abstract 3152 – Identification and characterization of inhibitors of SHOC2-MRAS-PP1C complex assembly

Identified inhibitors of SMP complex assembly via SHOC2 engagement, representing a potential new approach to attenuate RAS/MAPK pathway signaling. Genetic ablation or protein degradation of SHOC2 can sensitize RAS-driven cells to RAS/MAPK pathway inhibitors and prevent

adaptive resistance.

- Identified two lead series that bind selectively to SHOC2 with low nanomolar affinity, interfere with SMP complex assembly, and inhibit the SMP complex's phosphatase activity
- To our knowledge, these compounds represent the first examples of direct modulators of the SMP complex
- Further optimization of SHOC2 binders for protein-protein inhibitors (PPIs) and degrader modalities is ongoing

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 patients with 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 and early-stage development projects, including ERAS-0015, ERAS-4001, and our SHOC2 binding project; and our ability to achieve our goal of initiating the clinical development of ERAS-0015 and ERAS-4001 this year. 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 development of product candidates based on our singular focus on shutting down the RAS/MAPK pathway, a novel and unproven approach; results from preclinical studies not necessarily being predictive of future results; 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, 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; 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, 2024, 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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