Erasca Unveils First Clinical Candidates, Aims To Create A MAPK Clamp
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By Mandy Jackson

FORMER IGNYTA CEO’S WELL-FUNDED ERASCA OBTAINED its first clinical-stage precision oncology candidates from NiKang and Asana, eyeing a first-in-class approach to RAS/MAPK-driven cancers.

Erasca Inc. launched at the end of 2018 with $42m, a high-profile CEO and undisclosed precision oncology programs with the ambitious goal of “erasing cancer.” Even after raising another $200m in April of last year, the company founded and helmed by Jonathan Lim – who was heading up Ignyta, Inc. when Roche Holding AG agreed to buy it in 2017 for $1.7bn – declined to describe its cancer drug development programs. But now that Erasca has initiated its first clinical trial, the company is ready to unveil its first two drug candidates.

The San Diego-based company has accomplished a lot during the two years since its series A venture capital round. Including the series B mega-round last year, it has raised $300m to date and used its internal discovery platform to develop multiple cancer drug candidates. (Also see “Finance Watch: Erasca Raises $200m As VC Mega-Rounds Continue” - Scrip, 1 May, 2020.) And, as the company announced on 6 January, it has licensed and purchased exclusive worldwide rights to two externally discovered targeted cancer therapies and initiated its first clinical trial.

Erasca licensed the Src homology region 2 domain-containing phosphatase-2 (SHP2) inhibitor ERAS-601 from NiKang Therapeutics, Inc. and acquired the extracellular signal-regulated kinase (ERK) inhibitor ERAS-007 from ASN Product Development Inc., a wholly owned subsidiary of Asana BioSciences, LLC. Financial terms were not disclosed.

The company believes that both ERAS-601 and ERAS-007 are best-in-class compounds and intends to develop the two drugs in combination with each other, with internally developed candidates and with externally developed cancer treatments. Both candidates target upstream and downstream nodes in the mitogen-activated protein kinase (MAPK) signaling cascade.

By combining ERAS-601 and ERAS-007, Erasca believes it can create a clamp that blocks oncogenic drivers of tumor growth at both ends of the MAPK pathway to induce tumor regression and prevent drug resistance that can develop when treating RAS/MAPK-driven cancers.

The RAS/MAPK pathway is one of the most frequently mutated oncogenic pathways in cancer and patients with these mutations often have a poor prognosis, Lim noted in an interview with Scrip.

“There are some approved therapies against certain mid-pathway nodes in the MAPK pathway, such as BRAF and MEK, but the unmet need for patients with RAS/MAPK mutations still remains high as targeted therapies are available for only a subset of these patients,” he said.
“Creating a clamp that targets both upstream nodes like SHP2 and downstream nodes like ERK in the RAS/MAPK pathway could shut down the oncogenic drivers within this pathway, leading to a powerful anti-cancer effect.”

The RAS/MAPK pathway is associated with a broad range of cancers, including colorectal cancer (CRC), non-small cell lung cancer (NSCLC), head and neck cancer, pancreatic cancer, melanoma and other tumor types.

**Potential Best-In-Class SHP2, ERK Inhibition**

Erasca believes that preclinical studies it and NiKang conducted with the SHP2 inhibitor ERAS-601 show best-in-class activity against oncogenes upstream and downstream of SHP2 in multiple solid tumor types, including in NSCLC and CRC.

“ERAS-601’s profile enables us to explore doses that we predict will result in continual suppression of MAPK signaling,” Lim said, noting that the oral drug has ideal characteristics for daily dosing and combination regimens.

The best-in-class potential of ERAS-007 was illuminated by results from Asana’s Phase I clinical trial of the ERK inhibitor, which showed once-weekly doses could safely shrink tumors. Some of the patients in the monotherapy trial whose tumors had RAS- or RAF-mutated cancers had partial or complete responses to treatment.

“These data provide early evidence that ERAS-007 could be developed as a potential single agent for patients with certain oncogenic drivers that are sensitive to ERK inhibition,” Lim said. “ Combined, ERAS-601 and ‘007 target the proximal and distal ends of the MAP kinase pathway, thereby maximizing signal inhibition while minimizing potential opportunities for reactivation of the pathway by feedback loops.”

The first patient was treated in December in Erasca’s Phase I/IIb FLAGSHIP-1 study of ERAS-601 – the company’s first-ever clinical trial. The open-label, multi-center, dose escalation and dose expansion study will evaluate ERAS-601 as a single agent and as part of combination regimens in patients with advanced solid tumors. The endpoints include safety, pharmacokinetics, pharmacodynamic and anti-tumor activity.

“We are planning to initiate multiple monotherapy and combination therapy studies of ERAS-007 later this year,” Lim said. “We anticipate that we’ll have a recommended dose for ERAS-601 by next year. At that point we anticipate the combination evaluation of ‘007 could start shortly after that, so it will be in 2022 once the ‘601 recommended dose has been identified.”

Erasca’s strategy for developing the two drugs includes combining ERAS-601 and ERAS-007 with each other, combining each drug with candidates in the company’s drug discovery pipeline and testing them in combination with best-in-class and first-in-class agents that also target the RAS/MAPK pathway.

“We’re in dialog with multiple companies that have approved as well as investigational agents that could benefit from being combined with one or both of ‘601 or ‘007,” Lim said.

Erasca has raised a lot of cash to date but the CEO declined to reveal whether the company has immediate plans to raise capital for its planned ERAS-601 and ERAS-007 studies and to advance other internally developed or externally sourced drug candidates. He noted that “in just over two years we’ve raised $300m, so we’re well capitalized to pursue this strategy. Of course, rapidly growing biotechs need cash infusions so we will be actively looking to drive these programs forward with future financings.”

In addition to a large initial pool of cash, Erasca's management has proven experience successfully developing targeted cancer therapies. Less than two years after Roche acquired Ignyta, the San Diego firm’s kinase inhibitor entrectinib – now sold under the brand name Rozlytrek – gained US Food and Drug Administration approval to treat ROS1-positive metastatic NSCLC and metastatic solid tumors with a NTRK gene fusion. (Also see “Roche Ramps Up Cancer Portfolio With $1.7bn Ignyta Buy” - Scrip, 22 Dec, 2017.)

Rozlytrek generated CHF319m ($363.7m) in sales globally during the first nine months of 2020.