BIOCENTURY

REPRINT FROM AUGUST 23, 2021

EMERGING COMPANY PROFILE

Ranok: a chaperone-based approach to targeted degradation

BY PAUL BONANOS, ASSOCIATE EDITOR

An investor syndicate is backing Chinese biotech Ranok in a $40 million series B round that will allow the targeted protein degradation company to test its differentiated, chaperone-based approach in its first clinical trial.

Hangzhou-based Ranok Therapeutics Co. Ltd. is deepening its presence in the U.S. as it is poised to enter the clinic, founder and CEO Weiwen Ying told BioCentury. The biotech is preparing to conduct its first clinical trial in the U.S., and has a beachhead in Boston.

The company hasn't yet revealed the target or any planned indications for its most advanced program, which is built on Ranok's chaperone-mediated protein degradation (CHAMP) platform.

CHAMPs are heterobifunctional small molecules that share some traits in common with, but are differentiated from, the more commonly seen proteolysis targeting chimeras (PROTACs) used by several targeted degradation companies.

Both bind on one side to a target molecule, and steer it toward degradation by the ubiquitin proteasome system. But while PROTACs typically do so by binding directly to an E3 ligase, CHAMPs induce proximity to a HSP90 chaperone complex that includes multiple E3 ligases, CSO Kevin Foley told BioCentury.

Ranok believes the approach confers advantages over using PROTACs. Since HSP90 is highly activated in tumor tissues compared with normal tissues, CHAMPs are designed to have a higher therapeutic index and more on-target effects in tumors with fewer side effects in normal tissues, potentially offering a dosing advantage. Foley said the therapeutics may also be able to overcome resistance mechanisms associated with E3 ligase mutations, because the complex includes more than one E3 ligase.

In a presentation in April at the American Association for Cancer Research (AACR) virtual meeting that described degradation of BRD4 as preclinical proof of concept for the platform, Ranok said CHAMPs can also be used to degrade proteins not normally regulated by HSP90, such as mutated KRAS.

The biotech expects to reveal more about its lead program this year as it approaches the IND stage, and the round is designed to commence clinical work. Foley said plans for additional INDs could follow in the next year or so; the company is interested in treating both solid tumors and hematological malignancies.

CHAMPs are among several next-generation targeted degradation approaches that have emerged after a first wave of PROTAC companies, a handful of which have gone public.

Ranok has raised $50 million to date, including a $2 million seed round in June 2018 and a March 2020 series A that brought in more than $8 million. Lapam Capital and Shanghai Healthcare Capital led the new series B alongside Wu Capital, Zhongguancun Kaiyuan

COMPANY PROFILE
RANOK THERAPEUTICS CO. LTD.

Hangzhou, China

Technology: Chaperone-mediated targeted protein degradation

Origin of technology: Internally developed
Disease focus: Cancer

Clinical status: Preclinical

Founded: 2018 by Weiwen Ying, Kevin Foley and Junlin Wang

Academic collaborators: Undisclosed
Corporate partners: None

Number of employees: 14

Funds raised: $50 million

Investors: Lapam Capital, Shanghai Healthcare Capital, Wu Capital, Zhongguancun Kaiyuan Capital, TF Capital, Med-Fine Capital and LC Ventures

CEO: Weiwen Ying

Patents: None issued

Capital and prior investors. Ying said Ranok will seek to add U.S. investors in a future round.

Ying and Foley were both employees at Synta Pharmaceuticals Corp., which developed HSP90 inhibitor ganetespib. Following the 2015 termination for futility of a Phase III trial of that therapy in lung cancer, Synta was part of a reverse merger that made Madrigal Pharmaceuticals Inc. (NASDAQ:MDGL) the surviving entity.

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