Newco news

Degron raises $22M to develop molecular glue-based protein degradation platform

June 17, 2022
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Degron Therapeutics Inc. has raised $22 million in a series A round to develop its drug development platform, Gluexplorer. A molecular glue-based targeted protein degradation platform, Gluexplorer is used to speed up drug development in areas such as oncology, inflammation, metabolic disease and rare diseases, by combining a glue library and three screening techniques, including phenotypic screening, proteomic screening and artificial intelligence (AI).

"Small-molecule drugs have been the mainstay of disease treatments, but most disease targets remain undruggable," Lily Zou, Degron's co-founder and CEO, told *BioWorld*.

With phenotypic screening, researchers identify molecules that can kill cancer cells in an E3 ligase-dependent manner. They then identify which protein target is degraded by proteomic analysis, followed by confirmation of formation of E3-glue-target ternary complex.

Lily Zou, co-founder, and CEO, Degron

In proteomic screening, researchers use a mass spectrometer to identify proteins that are reduced in an E3 ligase dependent manner, then pick the targets that play essential roles in various disease indications.

The addition of AI helps predict targets and accelerate compound discovery.

Zou said she believes those three screening methods enable the firm to identify targets that cannot be predicted based on current knowledge of known glue substrates.

Shanghai-based Degron was founded in 2021. It was built on research and technologies developed by Degron's co-founder, Yong Cang, professor of Shanghaitech University.

"With our deep understanding of the mechanisms of actions of glue molecules and the tools and assays we developed, we think Degron can quickly advance targeted protein degradation drug discovery," said Zou.

With its Gluexplorer, Degron has developed a compound library and screening system for the development of small-molecule medicines. To date, the platform has yielded 20 programs of targets and degraders, three of which have been fully validated and advanced to the lead optimization stage, "in disease areas including cancer, inflammatory diseases and rare diseases," said Zou.

The most advance two candidates are a Wee1 kinase degrader and an undisclosed target protein A.

"We knew the limitations of small-molecular inhibitors on undruggable targets and had seen the challenges proteolysis targeting chimera (PROTAC) faced with their drug-like properties," Zou said. "As a result, we came to the conclusion that molecular glue is a breakthrough technology that could overcome the issues associated with PROTACs."

Molecular glue chemicals alter the substrate receptor surface of an E3 ubiquitin ligase non-covalently to allow recruiting of neo-substrates. PROTACs ligand both a ligase and a substrate to bring them to proximity.

"Small-molecule enzyme inhibitors mostly bind to a functional pocket of the enzyme to block its activity. However, the majority of disease targets, such as transcription factors and structural proteins, don't have such functional pockets and thus are deemed 'undruggable' by small-molecule inhibitors," said Zou.

Molecular glues can address that issue, she explained. "Molecular glues bind to either an E3 ligase or the target protein, altering the surface of one so that the other can bind to it. They serve as direct molecular adhesives between the ligase and the protein, and do not require a binding pocket on the target protein. As a result, they can target previously undruggable disease targets, which opens up many new mechanisms of treatment."

While a number of other companies are racing into the field, Zou said Degron is different from its competitors due to its "scaffold."

“The scaffolds that most companies use for their molecular glues are based on immunomodulatory drugs (iMiDs). Degron's scaffolds are structurally distinct from the iMiDs and serve as the starting point of our proprietary molecular glue library,” said Zou.

To date, the company has expanded its library to 6,000 compounds with 60 diverse scaffolds. Almost all of them are able to bind to an E3 ligase known as cereblon, which promotes protein ubiquitination and degradation.

“The structure of the glue molecule determines which target protein can be recruited, so the distinct Degron library allows us to discover targets that are differentiated from that of other glue companies,” said Zou.

The series A round was led by Med-Fine Capital. As part of the deal, Med-Fine partner Jing Yu joined Degron's board.

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BioWorld Cancer Series A China
KEYWORDS Degron Therapeutics Inc. molecular glues oncology protein degradation rare disease
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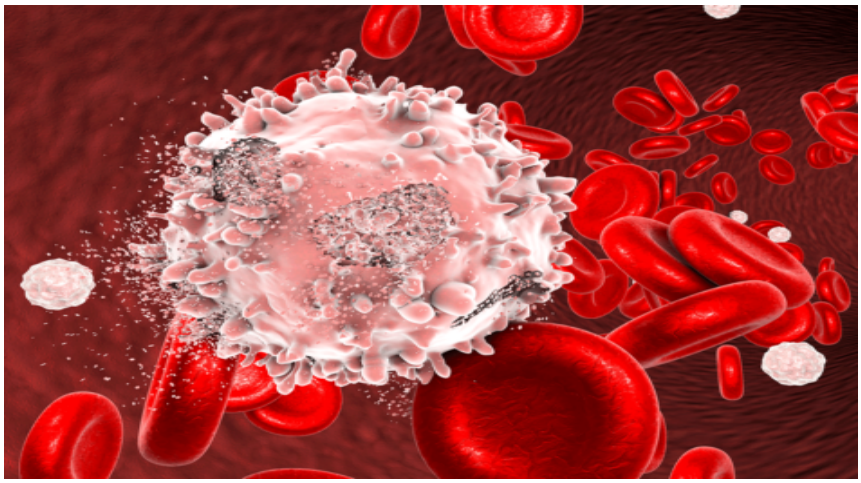

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