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Seagen And Nurix Hope To Pioneer A New Class Of Degrader-Antibody Conjugates

by Jessica Merrill

The two drug developers announced a collaboration to develop and commercialize multiple cancer programs. Nurix will receive $60m up front.

Seagen Inc. is teaming up with *Nurix Therapeutics, Inc.* on a broad multi-year, multi-target collaboration that aims to bring to market a new class of medicines for cancer called degrader-antibody conjugates (DACs). The companies announced the partnership on 7 September, with Seagen offering to pay Nurix $60m up front and potentially $3.4bn in milestone payments across multiple programs.

The partnership will combine Seagen's expertise in the field of antibody-drug conjugates (ADCs) with Nurix's work in the area of targeted protein degradation (TPD). The goal is to develop drugs with new mechanisms of action that combine the tumor specificity of antibodies with the targeted degradation of cancer-driving proteins.

"This is a very unique and strategic collaboration for the industry," Nurix CEO Arthur Sands said during a same-day call discussing the deal. "It represents a next-generation drug class for both TPD and the ADC field with a potential to improve treatment options for people suffering from a wide range of solid tumors and hematologic malignancies."

For Nurix, the deal also expands the use of its DELigase technology platform into the area of biologics and extends the company's cash runway through the second quarter of 2025, excluding any milestone payments. Nurix's drug discovery platform is focused on identifying small molecules that can decrease or increase protein levels, known as targeted protein modulation.

Seagen, a leader in the field of ADCs with several commercial drugs on the market, is poised to be acquired by*Pfizer Inc.*, though the companies are still awaiting regulatory clearance before the deal can close. Nurix said Pfizer was aware of the deal and had reviewed it as well.

Pfizer announced plans to acquire Seagen for $43bn in March, and while the companies are eager to advance Seagen's current pipeline, the focus is also on developing next-generation ADCs that can deliver improved efficacy and safety. (Also see "*Pfizer Pays $43bn For Seagen With Goal Of Rapidly, Globally Advancing ADCs*" - Scrip, 13 Mar, 2023.)

ADC technology has evolved over the years, but while the class of drugs has shown great promise in terms of efficacy, ADCs continue to be limited by toxicity. The compounds are complex drugs that bind a targeted antibody to a toxic payload through a linker system.

DACs would work in a similar way, but would use a linker to attach a degrader molecule to an antibody. Each antibody could have a payload of multiple degrader molecules attached to it, according to Nurix.

"As with ADCs, the antibody provides tumor tissue-specific delivery of the payload, the DAC," Sands said. "The unique aspect of the DAC is the nature of the payload, which is a highly engineered targeted protein degrader molecule." The approach could greatly increase the potential target universe of ADCs, he added.

"In addition, a single degrader molecule could be attached to multiple different antibodies providing a multiplicity of product opportunities," he said.

Under the terms of the collaboration, on top of the upfront and milestone payments, Nurix will be eligible for low double-digit tiered royalties on future sales of any products and the company retains an option for US profit sharing and co-promotion on two products arising from the collaboration. Nurix will be responsible for developing a suite of targeted protein degraders against multiple targets nominated by Seagen suitable to antibody conjugation. Seagen will be responsible for conjugating the degraders to antibodies to make DACs and for advancing the drug candidates into preclinical and clinical development.

More Validation For Nurix

Nurix is a pioneer in the emerging area of targeted protein degradation, which is one way drug developers are hoping to target disease-linked proteins that have long been viewed as being "undruggable." (Also see "*Scrip's Rough Guide To Targeted Protein Degradation*" - Scrip, 28 Feb, 2022.)

The company has three wholly owned programs in early clinical development, and also has collaborations with two other pharmaceutical companies: *Gilead Sciences, Inc.* and *Sanofi*. The San Francisco-based company went public in 2020. (Also see "*Protein Degradation Leader Nurix Prepares First Clinical Trial*" - Scrip, 15 Sep, 2020.)

Earlier this year, Gilead exercised its option to license Nurix's TPD molecule NX-0479, an oral

IRAK4 degrader for rheumatoid arthritis and inflammatory conditions, paying $20m up front. Under the original 2019 agreement, Gilead and Nurix agreed to collaborate on the development of up to five targeted protein degradation therapies. (Also see "*Gilead Dives Into Protein Degradation With Nurix Pact*" - Scrip, 20 Jun, 2019.)

Sanofi paid $55m up front to Nurix in 2020 to use its DELigase platform to develop small molecules designed to induce degradation of three drug targets, with an option to expand to a total of five targets.

Needham analyst Gil Blum, in a same-day note, said the latest deal with Seagen further validates Nurix's development platform.

"This collaboration, along with the existing agreements with Sanofi/Gilead, reinforce Nurix's DELIgase platform lead position in the TPD space," Blum said.

Leerink analyst Christopher Liu said the approach outlined by Nurix holds promise: "We believe this novel modality could improve the therapeutic window for certain highly active but toxic protein degraders, though clinical data will ultimately be needed to confirm the potential for these assets."