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BMS Spends \$100m On Orum's Antibody-Guided Protein Degradar

by Elizabeth Cairns

ORM-6151 combines two hot approaches in cancer R&D, but clinical trials have not yet started.

Today's deal between [Bristol Myers Squibb Company](#) and [Orum Therapeutics](#) is by no means the biggest over antibody-drug conjugates to have been signed this year, but is notable for the interesting combination of technologies it employs.

BMS has paid \$100m upfront to acquire Orum's ORM-6151, an anti-CD33 antibody conjugated to a degrader of GSPT1, a translation termination factor being explored as a therapeutic target for the treatment of acute myeloid leukemia (AML). The asset is still preclinical, though the US Food and Drug Administration has given its blessing to a Phase I study in AML or high-risk myelodysplastic syndromes.

Orum claims ORM-6151 is a first-in-class GSPT1 degrader, but this is not strictly accurate. BMS has previously discontinued two GSPT1 degraders of its own – both small molecules developed in partnership with Celgene. The US major canned the first, CC-885, a few years back owing to toxicity concerns, and switched to another similar product, CC-90009. However, in September this year BMS said it was also dropping CC-90009, again because of side-effect worries.

As an ADC, ORM-6151 could improve the therapeutic window over these past offerings by

Key Takeaways

- BMS pays \$100m upfront for ORM-6151, plus \$80m in potential milestones
- ORM-6151 is a GSPT1 degrader, like two discontinued BMS products
- Monte Rosa Therapeutics has a more advanced GSPT1 degrader

allowing precise delivery of the GSPT1 degrader payload to cancer cells.

At the American Association for Cancer Research meeting in April, Orum posted data suggesting that ORM-6151 had better efficacy than either CC-90009 or [Pfizer Inc.](#)'s CD33-targeting ADC Mylotarg (gemtuzumab ozogamicin), approved for AML in 2017, as well as showing minimal cytotoxicity to healthy hematopoietic progenitor cells.

The AACR data was all based on *in vitro* research, however, so the assertion of better efficacy and tolerability very much remains to be proven.

Moreover, there is another GSPT1 degrader ahead of ORM-6151. [Monte Rosa Therapeutics, Inc.](#) calls MRT-2359 a GSPT1 molecular glue degrader, and is already conducting human trials.

Monte Rosa has in fact reported interim data from the first 15 patients in a 133-patient Phase I/II trial of MRT-2359 in patients with a range of previously treated cancers, including lung cancer and high-grade neuroendocrine cancer. MRT-2359 significantly reduced GSPT1 protein levels in patients' tumors and showed evidence of tumor size reductions, including partial responses, in heavily pretreated patients.

Still, it might be unwise to get too excited about findings in so few patients. Full data from the study could come in 2026. In the meantime, one interesting question is why BMS plumped for ORM-6151 over Monte Rosa's more advanced asset.

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Perhaps price is the answer. The deal is small, with potential milestones coming to just \$80m. This is in sharp distinction to BMS's other ADC deal this year, in which a \$23m upfront payment to [Tubulis GmbH](#) could be followed by up to \$1bn in milestone payments, with royalties on top.

Even if those milestone payments were made in full the Tubulis deal would still come in way behind 2023's biggest ADC deal. The \$4bn [Merck & Co., Inc.](#) paid for licenses to three of [Daiichi Sankyo Co., Ltd.](#)'s candidates was the biggest upfront fee in pharma history. (Also see "[It's Official: The Merck-Daiichi Deal Has The Biggest Upfront Ever](#)" - Scrip, 23 Oct, 2023.)

A more intriguing deal might be the license [Seagen Inc.](#) – soon to be Pfizer – signed with [Nurix](#)

Orum Taking Novel ADC Approach To Protein Degradation

By [Jung Won Shin](#)

29 Jun 2021

Orum Therapeutics executives talk to Scrip on the next steps for the targeted protein degradation pioneer after a large-scale financing and on likely developments in the space in the coming years.

[Read the full article here](#)

Therapeutics, Inc. in September. This is a multi-year, multi-target collaboration based on Nurix's degrader-antibody conjugate technology. Neither the molecular targets nor the specific cancers the partners are working on have been disclosed.

ADCs are clearly a focus of furious activity – both in terms of R&D and dealmaking. Combining this approach with protein degradation could work; it is now up to BMS to prove it.

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