Interview with Ona Therapeutics

Antibody conjugates for drug resistant cancers

Following the trajectory of antibody-drug conjugates (ADCs) has never been easy. They are complex molecules with moving parts that don't always deliver the expected results in a clinical setting. An example of the challenges are the recent results of a Phase 3 trial of an ADC from Pfizer Inc for patients with lung cancer. On 22 June the company said the drug missed its primary endpoint. It said the comparator was challenging – a highly effective chemotherapy.

At the other end of the spectrum is the emergence of a diverse cohort of new ADCs with different structures and targets. One of the developers of these therapies is Tubulis GmbH, a German university spin-out that was acquired by Gilead Sciences Inc in May for up to $5 billion. The company has two ADC programmes in early clinical development, one for ovarian and non-small cell lung cancers, and the other for solid tumours.

A second example of a company that recently attracted capital is Ona Therapeutics SL, a Barcelona-based spin-out from two Spanish research institutes focused on helping patients with treatment-resistant cancers. Founded in 2019, Ona announced the closing of a $86.6 million Series B financing round on 4 June. This was led by Columbus Venture Partners and Mérieux Equity Partners. It followed a €30 million ($34.16 million) Series A round in June 2020.

In an interview on 15 June, Valerie Vanhooren, Ona's co-founder and chief executive, explained how Ona was able to advance a group of uncommon assets in a relatively short period of time. The company's lead product, ONA-255, is an ADC positioned to address refractory solid tumours. Initially this will be for patients with breast cancers that are hormone receptor-positive and HER2-negative, a particularly challenging patient population. The second portfolio product is ONA-389 for colorectal and hepatocellular carcinoma. A third, ONA-418, is a dual payload ADC that is in a holding position in the portfolio awaiting a further development of the market.

Dr Vanhooren holds a PhD in biotechnology from the University of Ghent in Belgium and gained her first R&D experience at Ablynx (now part of Sanofi SA), the developer of the nanobody, which is a single-domain antibody. "I always had a passion for oncology and at Ablynx I was learning the trade of making biologics and how to push a molecule forward from early-stage target identification," she said. This experience became important after Ona was launched and its first ADCs were being designed.

At the same time, the company's goal of addressing treatment-resistant tumours, meant that target discovery was crucial. After working at Ablynx, Dr Vanhooren moved to Spain where she led R&D at SpliceBio SL, a gene therapy company. This led to her immersion in the biotechnology ecosystems in Barcelona and the subsequent launch of Ona. The Ona team very quickly established relationships with hospitals in the area which were treating advanced cancers. The hospitals routinely took biopsies of cancers from patients with the disease – sometimes as many as 13 if the patient's cancer had relapsed over time. This guided treatment. Through collaborations, the Ona team was able to study tissue from relapsed cancers – specifically from the sites of tumour metastases.

"The targets that are present in the primary tumour are not always the same as the targets present on metastatic lesions," Dr Vanhooren said. Understanding this distinction, the company was able to identify a target – still undisclosed – that forms the basis of its technology platform. This is a target that is upregulated when patients become resistant to the standard of care. Moreover the Ona analysis has been confirmed in the US. "We do think that this is a global phenomenon," the executive said.

In 2020, not long after Ona's launch, Beatriz Morancho, a senior research scientist at the Vall D'Hebron Institute of Oncology in Barcelona joined the company as research director. In 2021, Haijun Zun, former head of antibody pharmacology at GSK Plc, became chief scientific officer. And in 2024 John Lambert, former chief scientific officer at ImmunoGen Inc, one of the first ADC developers, joined Ona's scientific advisory board.

It was the appointment of Antoine Yver in October 2025 as chair of the board of directors however that set the company on the path towards the clinic. Dr Yver has been tasked with accelerating Ona's candidate therapies to clinical inflection points. He has held executive roles at Daiichi Sankyo Co Ltd, Astra Zeneca Plc, Johnson & Johnson Inc and Merck & Co. Most importantly, he led the development of the Daiichi Sankyo, AstraZeneca ADC for breast cancer, Enhertu (trastuzumab deruxtecan).

In an email exchange after the interview, Dr Vanhooren confirmed that Ona plans to develop ONA-255 in patients with HR+ HER2-negative breast cancers. These cancers are being reclassified as HER2-low and HER2-ultra-low. "Despite recent advances there remains a substantial unmet medical need in this setting, particularly for patients whose disease continues to progress after available treatment options," she said.

The target identified by Ona for this patient population is not HER2. Rather it is another molecular mechanism that appears to address important unmet needs within the hormone receptor-positive breast cancer population. Dr Vanhooren added that "the patient population selected for development reflects where we believe the underlying biology is most relevant and where there remains significant opportunity to improve patient outcomes."

This article was written by the *MedNous* editor, Victoria English, and based on an interview and research on antibody-drug conjugates.