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Interview – With pivotal $105m ADC moves to copy its rivals

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Buoyed by its close rivals' swift clinical progress, ADC Therapeutics has secured a huge $105m funding round to push two of its antibody-drug conjugates into phase III trials.

The Geneva-based company reckons that these rivals have provided a blueprint for fast-tracking projects. The first clinical data on ADC's clinical assets – which target CD19 and CD25 – should emerge next year, and the company's chief executive, Chris Martin, tells *EP Vantage* that identifying "sub-disease cohorts" could allow for speedy development.

"We've observed what Seattle Genetics and Stemcentryx have done with their PBD-based ADCs [antibody-drug conjugates]. They went straight from phase Ib to registrational studies, so that's an approach we're aiming to adopt," he says.

Earlier this year Seattle started a phase III trial with vadastuximab talirine in older acute myeloid leukaemia patients. And Stemcentryx – subsequently bought by Abbvie for a huge $5.8bn – pushed into phase II with Rova-T in a very refractory subset of patients with DLL3-positive, small-cell lung cancer (*Abbvie caps week of cancer deals with huge Stemcentrx takeout, April 29, 2016*).

Both had previously been studied only in relatively small, early trials, and hope to win approval on the back of the ongoing studies owing to the lack of options in these patient groups.

Similarity

Four years ago ADC was spun out of Spirogen, which is now owned by Astrazeneca; the linker technology and PBD (pyrrolobenzodiazepine) toxic payloads that ADC uses for its conjugates were originally developed by its parent company (*Celtic invests $50m in antibody-drug conjugate start up, March 26, 2012*).

The Seattle and Abbvie assets also deliver a Spirogen-developed PBD-based payload.

Of course this similarity is not enough to guarantee the same swift progress for the Geneva-based drug developer. A clue to effectiveness will come next year with data from four phase I studies, testing the two agents, ADCT-402 and ADCT-301, in various settings in Hodgkin's and non-Hodgkin's lymphoma and acute lymphoblastic leukaemia.

ADCT-402 targets CD-19 using an antibody owned by ADC, while ADCT-301 targets CD-25 with an antibody licensed from Genmab.

Consciously coupling?

Linker technologies have long been considered a weakness of ADC approaches, but Mr Martin believes that this is in the past.

"The days of linker instability are behind us – mainly because of developments in understanding of what is a good linker and how to conjugate a drug. The challenge generally [for ADCs] is finding suitable targets and antibodies to those targets," he says.

CD19 certainly represents a crowded field. The leading CAR-T agents are CD19 targeted, as is Blincyto, the bispecific antibody launched by Amgen last year, and several ADCs and follow-on bispecifics.

Mr Martin acknowledges that he will be targeting the same patient groups as CAR-T therapies, but believes that the conjugates will represent a very different proposition.

"We could administer at the bedside as soon as the patient is diagnosed. And we believe the side-effect profile is going to be favourable compared with CAR-T. We believe it will be fairly complementary," he says.

The money

ADC now has enough cash to get into pivotal programmes with ’301 and ’402, at which point partnering efforts will probably commence, Mr Martin says.

The new funds will also allow it to participate in a collaboration it has with Astrazeneca over ADCT-401, which targets the antigen PSMA in prostate cancer. This and another preclinical pipeline candidate should enter the clinic next year.

The funding is not insignificant: it ranks as the seventh-largest private round by a European drug developer over the past 10 years, according to *EvaluatePharma*. However this is apparently not a pre-IPO round.

“We maintain ourselves IPO-ready, but we have no imminent plans to do so,” Mr Martin insists.

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