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Cumulus raising $50M, spinning GPR68 small molecules into GIO

By Nuala Moran, Staff Writer

Cumulus Oncology Ltd. is in the thick of raising a $50 million series A round as its model of sourcing novel drug targets emerging from academia, shaping them up for clinical development, and spinning them into startups, gathers pace.

At the same time, Nodus Oncology Ltd., the first spinout created around an acquired asset, has just reached in vivo proof of concept with its lead DNA damage response (DDR) inhibitor, and it, too, is looking to raise a series A to take the program through to the end of phase I.

Clare Wareing, founder and CEO, Cumulus Oncology

The progress made by Nodus following its formation two years ago to take on novel DDR targets, is one spur for Cumulus to raise a series A. Another is reaching a key milestone in drugging the proton-sensing G-protein couple receptor, GPR68, which plays a crucial role in tumorigenesis, tumor growth and metastasis.

Cumulus says it has discovered a series of selective and potent small molecules against GPR68, which it is moving into an accelerated optimization phase.

This program will then be placed in Cumulus' second spinout, GIO Therapeutics AG, which will also be the repository for other GPCR programs, both in oncology and inflammatory diseases. (GIO stands for GPCRs in Inflammation and Oncology).

Another spinout, Nuanbio Ltd., will specialize in developing antibodies and antibody-drug conjugates that target novel antigens, with the aim of disrupting tumor metabolism and signaling pathways.

A fourth, as yet unnamed spinout, aims to discover inhibitors of GTPases that control various cellular processes that are dysregulated in cancer cells. Although well recognized as being involved in tumor development and progression, GTPases have proved very hard to drug, and Cumulus is using new molecular simulation tools in its effort.

While the model of sourcing academic assets and advancing them to the point of being investible for venture capitalists is well established in the U.S., Cumulus claims it is the only oncology specialist taking this approach in Europe.

"The business model in the U.S. is very well established. In Europe, there's not as many of us doing it. But I think there's a momentum about the model and a recognition that actually it's a very capital efficient way to do drug discovery and drug development," said Cumulus founder and CEO Clare Wareing.

"Our model is to derisk science at the Cumulus level. We will fund quite a lot of research until the point where we think 'this has got legs.' At that point we will spin it out into a new company," Wareing said.

"The reason I started the company and chose to do it this way was to enable us to terminate projects early. For us, we only keep going if the data tell us to keep going; terminating projects early, I think, leads to better success rates later," she told *BioWorld*.

At its formation in 2017, it was difficult to raise money around the concept of taking raw academic research on targets and translating that into drug discovery and development programs, but Edinburgh, U.K.-based Cumulus has now raised £20 million (US$26.3 million) in seed funding, most recently in a £9 million round in January 2024.

"The initial investors backed an idea. And yet, here we are, three rounds later and we've got to a real milestone in GIO Therapeutics, the in vivo proof of concept on Nodus, and other projects being derisked at the Cumulus level," Wareing said. "We've really proven the impetus for future development is there."

Characterizing GPCRs

In the case of GPR68, Cumulus' interest was sparked both because GPCR targets are under-represented in oncology drugs and because it is now possible to stabilize GPCRs in situ straddling the cell membrane, and to characterize them more effectively.

"We spend a year or longer looking at what GPCRs were out there and what data there was," said Wareing. That included a global search of academic labs which generated 80 proposals. During research to whittle down this list, GPR68 "kept coming up again and again," and "there was lots of validation in the literature," she said.

The GPR68 assets were generated in a collaboration between Cumulus and Leadxpro AG of Basel, Switzerland, a specialist

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in structure-based drug discovery for membrane proteins, which solved the high resolution protein structure, informing compound design.

Cumulus announced last week that it was licensing the small molecules and associated IP, and for now will continue to fund the program. "We want to make sure that at the time we put it into GIO it's with the right data package for it to be investible and for us to bring other investors into the mix. We know what data they're looking for; we know we got to produce in vivo proof of concept," Wareing said.

That is the position Nodus's lead program has reached, prompting moves to raise a series A for the spinout and move into clinical development. The program is a poly (ADP-ribose) glycohydrolase (PARG) inhibitor which was acquired from Basilea Pharmaceutica Ltd.

Although a close relative of PARP, which is the target of inhibitor drugs including Astrazeneca plc's blockbuster Lynparza (olaparib), the therapeutic potential of PARG has been largely ignored. That is despite it acting in the same pathway as PARP to promote repair of double and single strand DNA breaks.

Expression of PARG is upregulated in many cancers and its activity is known to have an impact on cancer cell resistance to PARP1 inhibition.

While not attracting anything like the level of attention of PARP, there are other PARG programs in early research. The most advanced of these is Ideaya Biosciences Inc.'s IDE-161, which is in phase I, with the company announcing earlier this month that selection of an initial Phase I/II monotherapy expansion dose in homologous recombination deficient solid tumors remains on track for the second half of 2024.

"Our product acts on the same pathway, but it does it in a very different way," said Wareing. "Our data is every bit as good. We've done comparative [preclinical research] against IDE-161; we've got very strong in vivo proof of concept."

There is a lot of interest from both pharma companies and investors. "We're waiting for clinical validation [of IDE-161]. If there's an asset that has a clinical signal, all of a sudden that asset class becomes very desirable," Wareing said.