Evaluate Vantage

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Orbital shows 2023’s venture funding scene is far from stratospheric

Madeleine Armstrong

The group’s $270m series A, big for 2023, is not that impressive compared with other years.

Despite scepticism from public investors around advanced therapies, developers of cutting-edge technology can still haul in the big bucks from venture investors. This was shown when the RNA specialist Orbital Therapeutics scored a $270m series A round last month, marking the largest VC fundraising for a western biotech in 2023 to date.

However, a closer look at big rounds in previous years suggests that this total is not much to write home about. With funds being more selective about where they put their cash it is hard to see this situation changing dramatically over the year.

Top-five biopharma VC rounds in 2023*

Company	Series	Value ($m)	Date
Hasten Biopharmaceutic	Series A	315	20 Apr 2023
Orbital Therapeutics	Series A	270	26 Apr 2023
Cargo Therapeutics	Series A	200	9 Feb 2023
Aera Therapeutics	Undisclosed	193	16 Feb 2023
Torl Biotherapeutics	Series B	158	13 Apr 2023

**Up to 5 May 2023.*

There were some other decent sums raised in April, with China’s Hasten hitting the top of the charts, and the cancer specialist Torl bagging a $158m series B. The latter is developing antibody-drug conjugates hitting Claudin6 and Claudin18.2, with both the modality and targets being hot right now.

Still, these pale into insignificance when pitted against the top rounds since 2018.

Top-five biopharma VC rounds since 2018*			
Company	**Series**	**Value ($m)**	**Date**
Altos Labs	Undisclosed	3,000	20 Jan 2022
Suzhou Abogen Biosciences	Series C	700	23 Aug 2021
Sana Biotechnology	Series A	700	23 Jun 2020
Curevac	Undisclosed	640	21 Jul 2020
Eqrx	Series B	570	11 Jan 2021
**Up to 5 May 2023.*			

As for Orbital, its chief executive, Giuseppe Ciaramella, tells *Evaluate Vantage* that the group is working on both linear and circular messenger RNA, alongside two potential methods of delivery: lipid nanoparticles (LNPs) and virus-like particles (VLPs).

The linear RNA and LNP technology come from the base editing specialist Beam Therapeutics, with which Orbital has close ties: Ciaramella is also president of Beam. And the circular RNA and VLP knowhow comes from Stanford University, the former via a company called Circbio, which Orbital acquired last autumn.

It is hoped that circular RNA could improve durability versus linear RNA, which is susceptible to degradation from its open ends. But Orbital is not the only group pursuing this technology: Merck & Co last year signed a deal with Orna, and various others are also in the space.

Orbital is also looking at ways to stabilise linear RNA and improve its durability, according to the chief exec.

Choosing which technology to use will depend on the disease in question, and this “toolbox” approach is a big selling point of Orbital, Ciaramella says. He eschews the idea of taking “the next shiny tool and building a company around that”.

“A company that just has one technology has to make that technology work. It's difficult to have the magic silver bullet that does everything well,” he says.

This is also true of delivery, where Orbital is again hedging its bets. LNPs have traditionally been used to take cargoes to the liver, while VLPs could help expand RNA’s use into other organs. However, Ciaramella reckons LNPs have broader potential, too, and Orbital has access to Beam’s so-called “barcoded” LNPs that could go beyond the liver.

Three pillars

Ciaramella will not give details on what diseases Orbital will be working in, but points to three pillars the group will be built around: next-generation vaccines, protein-replacement therapy, and in vivo immunobiology.

The last pillar could include in vivo Car-T, and here Ciaramella highlights autoimmune disease as a particularly exciting application. “We can use Car-T to essentially reset the immune system so that we eliminate the memory of making antibodies against self-antigens.”

This is an increasingly hot space: Novartis has made no secret of its interest here, and other big pharma names are also looking at this use. But Ciaramella believes that the in vivo approach could have advantages, such as avoiding the chemo conditioning needed with ex vivo Car-T. “Chemotherapy can be acceptable in oncology, but it’s really not acceptable in the autoimmune space.”

Ciaramella estimates that the first Orbital project could hit the clinic in two to four years. “I suspect some of the vaccine applications as well as some of the protein replacement therapies that we have in mind are probably going to move a little bit quicker.”

He adds: “These pillars have been chosen because they have very different risk profiles. In some cases it's easier to deliver but maybe the biology [is] more complicated, and vice versa.”

This is “very deliberate”, he says. “One has to be humble when you start with a relatively new platform, because it's easy to pick the wrong areas to focus on very early on, and then you potentially compromise the success of the entire platform. By doing it in these pillars, we create the opportunity that at least, if one is not successful, the other two might be.”

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