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Ovid takes a novel approach to gene therapy

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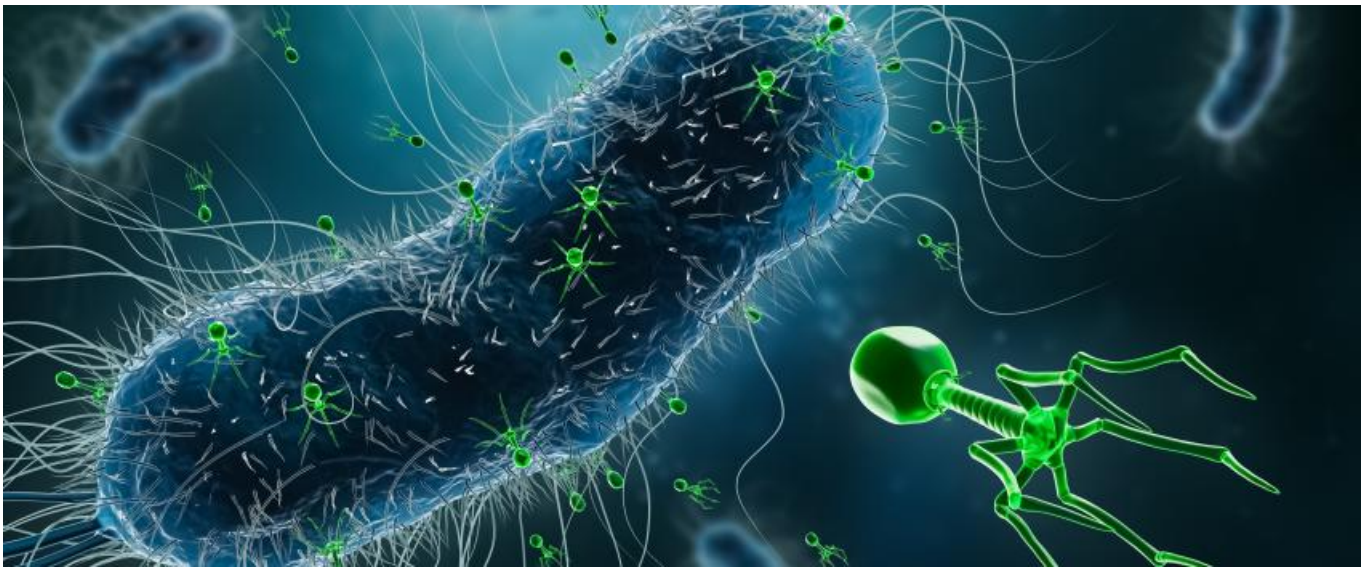

Ovid and its partner Gensaic have high hopes for a brand-new delivery method, and much to prove.

A tough couple of years has not stopped the rare epilepsy specialist Ovid Therapeutics from investing in gene therapy, an area that has proven the kiss of death for many other companies. The group hopes that, in Gensaic, it has signed up a partner that could help it tap into the next big thing: gene therapy delivered via phages, viruses that infect bacteria.

Ovid believes that phages could avoid many of the problems that have dogged mammalian viral vectors like adeno-associated viruses (AAVs), which are commonly used in gene therapies. Still, with the technology at the early preclinical stage, the question could be whether Ovid can keep going for long enough to make its gene therapy dream a reality.

And Ovid is dreaming big. It is homing in on central nervous system indications, where AAV-delivered gene therapies have previously run into problems. “We want to revolutionise brain disease,” says Jeremy Levin, who is Ovid’s chief executive officer as well as chairman of Gensaic.

Epilepsy and beyond

The initial focus will be epilepsy, “but should we see another opportunity that's viable we'd be foolish not to do it”, he tells *Evaluate Vantage*. The agreement covers up to three genetic medicines for unnamed CNS indications.

As part of the collaboration, Ovid will make a $5m investment in Gensaic, a private group that was spun out of MIT last year and is also known as M13 Therapeutics.

In the meantime, Gensaic has been building its intellectual property base; Mr Levin says he is not aware of any companies doing anything similar.

Phages are naturally harmless to humans, something that should give them an advantage over current gene therapy delivery technologies. A major drawback of AAV vectors is their immunogenicity, which is often countered with steroids. Meanwhile, “the evidence to date suggests that [phages] will not engender an immune response”, says Mr Levin.

This lack of immunogenicity should allow redosing with phage-based gene therapies – something that others are also trying to achieve with alternative delivery methods, such as lipid nanoparticles (LNPs).

Another plus with phages is their ability to carry large cargoes, a feature shared with LNPs. Finally, they should be easier and cheaper to manufacture than AAVs and even LNPs, he says.

Tissue targeting

The inert nature of phages means that Gensaic has had to engineer its capsids to spur uptake into host cells and expression of the genetic payload. “Think of it like a beacon that tells it how to interact with your cell,” says Gensaic’s chief executive, Lavi Erisson.

Another modification involves adding a targeting moiety to the capsid, allowing therapy to be directed to specific locations in the body. This could provide another advantage over both AAVs and LNPs, which tend to accumulate in the liver.

For CNS disorders it will be important for the phage-based vectors to get into the brain. Poor penetration with AAVs has led companies to try direct brain delivery in CNS disorders, resulting in toxicity concerns; some groups are trying to boost brain targeting with AAVs to improve the therapeutic window with intravenous dosing.

Mr Levin believes that phages naturally cross the blood-brain barrier, and this is something that will be put to the test.

Outside the brain

While Ovid is squarely focused on CNS diseases, Gensaic could have much broader appeal, with its vectors potentially able to target any organ. The company also says the phage-derived particles could be developed for oral, inhaled, intravenous and intrathecal administration.

According to Mr Erisson, Gensaic is talking to “at least four” other possible partners, but wants to limit itself to around three deals in the next year or so; the group also plans to advance its own internal pipeline.

As for Ovid, since the failure of its Angelman project OV101, its most advanced asset is soticlestat, but this is now being developed by Takeda. The company, whose other contenders have not yet hit the clinic, reckons its current $150m cash reserves will get it into 2025.

Gensaic’s phage-derived particles are unlikely to move the needle for the group for now. Mr Levin sees gene therapy as a long-term play, but impatient investors might not be prepared to wait around if other projects fall by the wayside.

To read Evaluate Vantage’s report into next-generation genetic medicines, click here.