‘Holy grail’ of gene therapy still a long way off for cystic fibrosis

Drug development

Conventional treatments developed by Vertex can now help many sufferers, but they have a hefty price tag, says David Crow

Until six years ago, there was nothing that could stop the relentless march of cystic fibrosis, a relatively rare disease that affects roughly 75,000 people worldwide, which causes the build-up of thick mucus in the lungs, pancreas, and other organs.

Sufferers did not expect to see their 40th birthday: after years of battling persistent infections since childhood, most succumbed to fatal lung disease.

The frustratingly slow progress was surprising given that the gene responsible for cystic fibrosis was discovered in 1989, well before the understanding of other hereditary diseases was unlocked by the completion of the human genome project in 2003.

The early finding raised hopes that the disease could be tackled with a gene therapy, a one-off intervention that would correct the defect in the cystic fibrosis gene at source.

But, as with other early attempts at gene therapy, the efforts were fruitless.

“Way back in 1989, it turns out we weren’t ready for a gene therapy approach,” explains Paul Negulescu, a senior vice-president at Vertex, which makes medicines that can arrest the development of cystic fibrosis.

“It resulted in a gap in the 1990s for cystic fibrosis,” he adds. “It could be longer than that: the holy grail lies in exploring the gene therapy approach that was tried in the 1990s, which could theoretically cure the disease.

But Dr Leiden, whose company is working on an approach, warns the challenges remain formidable.

That is because the only gene therapy to win approval in the US — Luxturna for childhood vision loss — is delivered by injection directly into the eye.

The lung, however, has a surface area that is more than 50 square metres, and scientists have not come close to working out how to deliver a gene therapy to such a large organ.

Even if it were possible, it would not solve the damage that cystic fibrosis does to other organs like the liver and pancreas.

“We believe it is probably the ultimate answer,” says Dr Leiden. “We’re working on it hard, but it’s a 10- or 15-year problem.”

Prices are unlikely to fall soon, in part because there are no viable competitors to Vertex on the immediate horizon.

The closest possible rival drug is being developed in a collaboration between Galapagos, a biotech group, and AbbVie, a Big Pharma company. However, analysts say the pair are significantly behind Vertex.

Vertex’s recent announcement that it plans to start trials of a triplet drug in the first half of this year “could further limit opportunities for competitors”, says Geoff Meacham, an analyst at Barclays.

Despite the big advances using traditional pills, some companies believe the holy grail lies in exploring the gene therapy approach that was tried in the 1990s, which could theoretically cure the disease.

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Since then, Vertex has managed to boost the number of patients who can benefit from treatment by combining ivacaftor with other medicines and today the company’s drugs help a little over half of cystic fibrosis sufferers.

The next big step is the development of so-called triplet drugs that combine three separate medicines in one tablet. Vertex will soon start two late-stage trials of different triplets, which could produce a viable drug, taken by mouth, that you could help the patient recover and improve,” recalls Mr Negulescu.

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Because the disease progresses slowly, it will take years to find out whether Vertex’s medicines can boost life expectancy, although recent mid-stage studies showed its triplets led to a 13 to 14 per cent improvement in an important measure of lung function.

“Patients can feel that immediately,” says Mr Negulescu.

“Long term data shows that we are cutting the rate of progression at least in half... our goal is a normal lifespan.”

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