AviadoBio
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AviadoBio: revolutionary gene therapies for neurodegenerative disorders

By taking a neuroanatomy-led gene-therapy approach, AviadoBio is developing targeted drugs and delivery technologies to advance the treatment of neurological conditions such as frontotemporal dementia and amyotrophic lateral sclerosis.

Neurological diseases are the single largest cause of disability worldwide and the second leading cause of mortality. Although genetic medicine has great promise for treating these disorders, physiological barriers have thwarted effective delivery, and safety issues exist with common routes of administration.

AviadoBio is a central nervous system (CNS) gene-therapy company pioneering novel applications to slow and potentially arrest neurodegenerative diseases. The company has developed novel gene-supplement and gene-silencing platforms targeting the genetic drivers of monogenic and complex neurodegenerative disorders. This is complemented by pioneering surgical-delivery solutions to maximize biodistribution.

"As a neurologist, I've been seeing patients with dementia and amyotrophic lateral sclerosis (ALS) for more than 30 years, and there have been very few new therapies, despite significant progress in identifying genes and understanding disease mechanisms," explained Chris Shaw, AviadoBio CSO and co-founder. "One key lesson is that successful treatment relies just as heavily on how a gene therapy is delivered as on its efficacy. Our deep understanding of brain anatomy and unique delivery technologies allow us to deliver the right amount of the right drug to the right place for maximum effect, while limiting peripheral organ exposure."

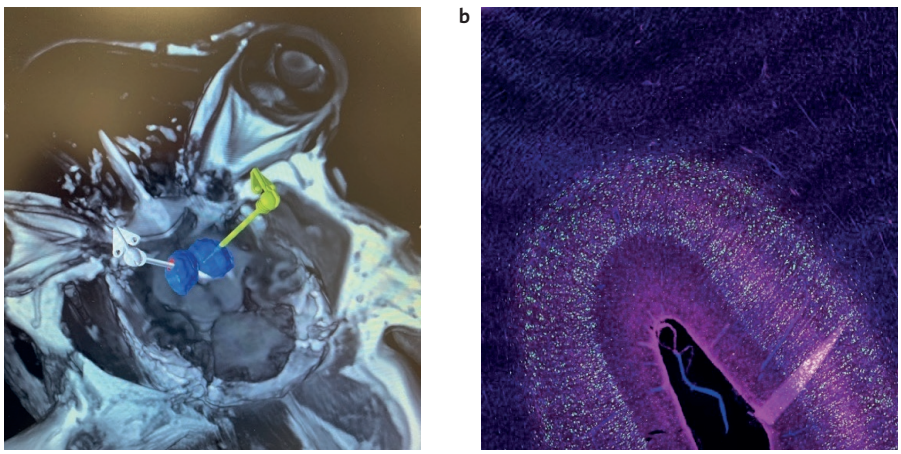

Fig. 1 | Intrathalamic gene therapy delivery in sheep. a, MRI image of sheep skull demonstrating simulated bilateral intrathalamic infusion (blue) into brain. **b**, Immunofluorescent imaging of prefrontal cortex in a sheep treated with intrathalamically-delivered PGRN AAV gene therapy (PGRN protein in purple, neurons in green). AAV, adeno-associated virus; PGRN, progranulin.

Promising targets for frontotemporal dementia and ALS

AviadoBio is advancing a pipeline of investigational therapies and delivery devices for neurodegenerative diseases, with an initial focus on frontotemporal dementia (FTD) and ALS.

Lead candidate AVB-101 is in development for treating FTD that is caused by loss-of-function mutations in the progranulin gene *GRN*, known as FTD-*GRN*, which is a devastating early-onset dementia that typically affects personality, behavior, and language. AVB-101 delivers the *GRN* gene by infusion directly into the thalamus, driving GRN protein production, which is distributed along axonal networks and secreted throughout the brain. AVB-101 is a single treatment designed to halt disease progression and has the potential to prevent FTD caused by *GRN* mutations.

"When gene therapies are delivered into the bloodstream or spinal fluid the hope is that they reach the brain, but fewer than 1% of cortical neurons become transduced," said Shaw. "In contrast, intrathalamic delivery of AVB-101 in sheep and non-human primates was well tolerated and achieved human physiological levels of human progranulin (hPGRN) throughout the brain" (Fig. 1).

AVB-101 has been granted orphan designation by the US Food and Drug Administration (FDA) and European Commission, and the phase 1/2 ASPIRE-FTD study was recently opened for enrolment in Europe.

Simultaneously, AviadoBio is exploring its subpial delivery technology for neurological diseases involving the spinal cord. These include ALS—a rapidly progressive neurodegenerative disease that leads to progressive paralysis and death in 3–5 years from symptom onset. Among the company's ALS portfolio is a gene-silencing therapy that is delivered to the spinal cord via a single injection under the surrounding pial membrane.

"Subpial delivery has the potential to allow significantly lower doses of gene therapy to be delivered to the spinal cord of patients in a one-time, minimally invasive procedure, providing broad biodistribution along the spinal cord, and potentially addressing safety concerns," said Shaw. "We believe this could be a ground-breaking advance in the treatment for ALS and other neurological spinal disorders."

Partnering to advance next-generation approaches

AviadoBio's industry-leading science and technology are founded on pioneering research from King's College London and the UK Dementia Research Institute. This rich heritage in academia is complemented by a strong leadership team with extensive gene-therapy development and commercialization experience and is supported by a syndicate of top-tier investors.

The company is using internal research and development and external collaboration for additional therapy and delivery efforts, and is open to strategic partnerships that align with its mission of delivering highly effective treatments to patients. "We are building world-class capabilities to discover, develop, manufacture, and commercialize gene-therapy products. Our neuroanatomy-led approach to drug delivery should have utility across many neurological diseases involving the brain and spinal cord," said Lisa Deschamps, CEO. "Tackling dementia and ALS has proved enormously challenging. We are uniquely positioned to identify and overcome the challenges with today's gene therapies and advance the field by combining precise genetic medicines with targeted delivery solutions that get the drugs directly to the brain and spinal cord, while minimizing off-target effects. Our team is relentless in this pursuit of transforming the lives of patients and families living with devastating neurodegenerative disorders, and looks forward to collaborating with partners, physicians, patients, and care partners in these efforts."

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