



4BIO Capital’s review of AAV gene therapy clinical trials published in *Nature Reviews Drug Discovery*

Systematic review and meta-analysis of 149 clinical trials of AAV-based gene therapies demonstrates high safety and efficacy rates

Data reinforces potential of AAV-based gene therapies to become a mainstream and potentially curative treatment modality

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LONDON & BOSTON – 4BIO Capital (“4BIO” or “the Group”), an international venture capital firm focused solely on the advanced therapies sector, announces the publication of a systematic review paper entitled “[The Clinical Landscape for AAV Gene Therapies](#)” in *Nature Reviews Drug Discovery*.

The review, led by Dr. Dima Kuzmin in collaboration with academics from the University of Oxford and Children’s Hospital of Philadelphia as well as several members of 4BIO’s management and advisory teams, analyses 149 unique adeno-associated virus (AAV) gene therapy clinical trials, determining current key trends and depicting the impact of clinical trials on the gene therapy field. This is the first systematic review and meta-analysis that establishes transition probabilities, cumulative safety, and efficacy data for AAV gene therapies.

Gene therapy using AAV as a vector has emerged as a novel therapeutic modality with significant clinical developments made over the past 20 years, including the treatment of over 3000 patients, showing its potential for substantial disease modification in many monogenic disorders, and perhaps even cures. The most commonly used serotype, AAV2, has produced vast amounts of safety and efficacy evidence, indicating its ability to be readily used within the gene therapy space. In addition, decreasing clinical trial duration, which reflects increased comfort from regulators, and the growing number of successful clinical trials focusing on treating diseases of the central nervous system (CNS), reiterates the potential of AAV gene therapy as a safe, well tolerated and efficacious therapeutic modality.

The authors show that AAV gene therapy is generally safe and well tolerated, with no clinical trials failing to reach their primary safety endpoints prior to the cut-off date of the review. Additionally, whilst sample sizes are still relatively small, the existing data indicates the success rates of gene therapy development are significantly higher than the average for all modalities. For example, the transition probability for a drug progressing from an investigative new drug (IND) to a new drug application (NDA) is 31% for ophthalmology gene therapies as compared to 24% across all modalities; 43% vs. 16% in metabolic diseases; 56% vs 47% in haematology; and 30% vs. 19% in neurology.

However, the authors conclude that drawbacks remain and further innovations, such as better manufacturing, an ongoing switch to engineered capsids and synthetic promoters could lead AAV gene therapies to advance from the primary targets of the retina, liver, muscle and brain into other major organs and therefore into the next stage of clinical significance.

Dr. Dima Kuzmin, Managing Partner at 4BIO Capital, said: *“The analysis of vast amounts of clinical trial data has allowed us to establish the safety, tolerability and efficacy of AAV gene therapy, and consider it as a potential curative modality. Whilst certain challenges, such as uncertainty with regards to durability of response to gene therapy and potential viral vector liver toxicity are still yet to be overcome, it is clear that AAV gene therapy has the potential to become an effective mainstream therapeutic option.”*

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About 4BIO Capital

4BIO Capital is an international venture capital firm focused solely on the advanced therapies sector.

4BIO’s objective is to invest in, support, and grow early stage companies developing treatments in areas of high unmet medical need, with the ultimate goal of ensuring access to these potentially curative therapies for all patients. Specifically, it looks for viable, high-quality opportunities in cell and gene therapy, RNA-based therapy, targeted therapies, and the microbiome.

The 4BIO team comprises leading advanced therapy scientists and experienced life science investors who have collectively published over 250 scientific articles in prestigious academic journals including *Nature*, *The Lancet*, *Cell*, and the *New England Journal of Medicine*. 4BIO has both an unrivalled network within the advanced therapy sector and a unique understanding of the criteria that define a successful investment opportunity in this space.

For more information, please visit www.4biocapital.com