Progress of gene therapy to treat Rett Syndrome.

This brief article is a follow-up to previous articles now on the RSAA website (https://rettaustralia.org.au/blog/novartis-and-gene-therapy-to-treat-rett-syndrome/ AND https://rettaustralia.org.au/blog/adeno-associated-virus-aav-as-a-delivery-vehicle/).
A recent webinar entitled "Gene therapy for rare diseases" from the International Rett Syndrome Foundation chaired by staff member, Dr Dominique Pichard, was presented by Dr PJ Brooks [National Centre for Advancing Translational Sciences (NCATS)] and Dr Jill Jarecki (Cure SMA-spinal muscular atrophy). Dr Brooks presented the NCATS strategy to develop adeno-associated virus (AAV)-related gene therapy for 4 rare diseases, none of which is Rett Syndrome. However, these studies are expected to generate novel data applicable to gene therapy for Rett Syndrome itself. To complement Dr Brooks' presentation, Dr Jarecki presented a summary of previous clinical trials of gene therapy for SMA as reported in the literature by Novartis.
Dr Brooks noted that the role of NCATS was to develop a single AAV platform that could be used by many researchers. This strategy is designed to identify which of the 9 strains of AAV is most appropriate for the delivery of functional genes to cure rare diseases. The outcome of these studies is expected to considerably reduce the cost when applied to other specific gene therapy strategies, including Rett Syndrome.
Dr Jarecki outlined a number of important points for the success of AAV gene therapy for SMA developed by Novartis and considered how these might be applied to Rett Syndrome. Despite this success, there was still a spectrum of responses, probably related to the initial severity of the condition, to the age of the patient or other as-yet unknown factors. This information is vitally important for future efforts to cure Rett.
These studies provide additional optimism for positive outcomes of AAV-related gene therapy for Rett Syndrome. Two companies in the USA, Novartis and Acadia, intend to submit an application for an Investigational New Drug (IND) to treat Rett Syndrome to the US Food & Drug Administration (FDA) by the end of 2021. This application will include recent data on the results of preclinical studies including safety and efficacy, and details of any proposed clinical trials. These trials are expected to clarify several factors including the likely dose of AAV-MeCP2, the age of participants and other features related to the specific MeCP2 mutation. The SMA experience and expertise gained by Novartis is likely to accelerate approval for Rett Syndrome gene therapy, provided the results of any clinical trials are encouraging.
The field may appear to move slowly, but researchers and clinicians must tread carefully to ensure safety, as failure to do so has the potential to set the field back by several years.
Basic information on gene therapy is available on the American Association for Gene and Cell Therapy website (https://asgct.org/) and can be accessed under the education page.

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