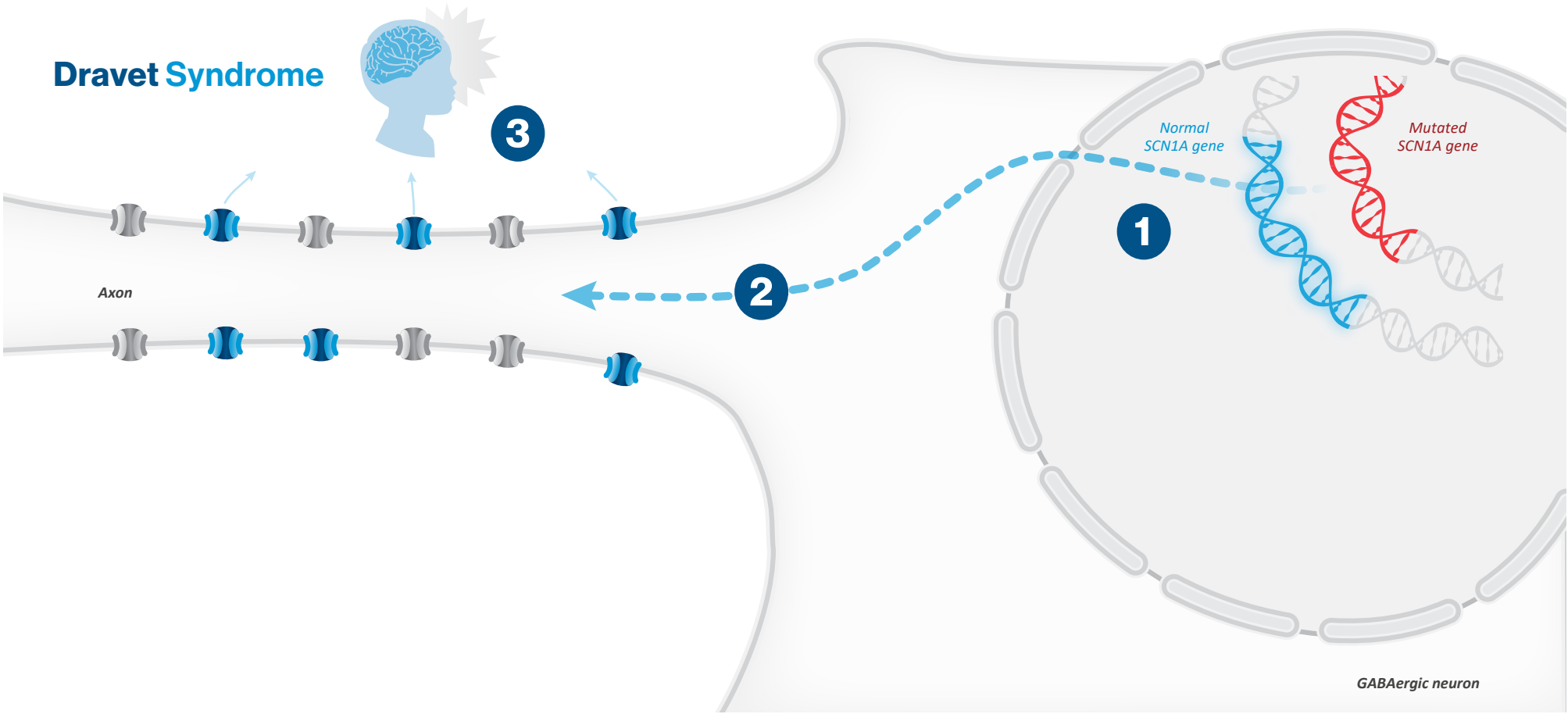
Encoded THERAPEUTICS

How **ETX101 Works**

Dravet Syndrome



1 Mutation in a single copy of the 6kb SCN1A gene, which codes for the voltage-gated sodium channel NaV1.1 (haploinsufficiency)

2 Decreased expression of NaV1.1 leads to lower sodium channel activity and reduced GABA release.

3 GABAergic inhibitory neuron dysfunction causes uninhibited cortical excitation, leading to epileptic seizures and affecting cognition

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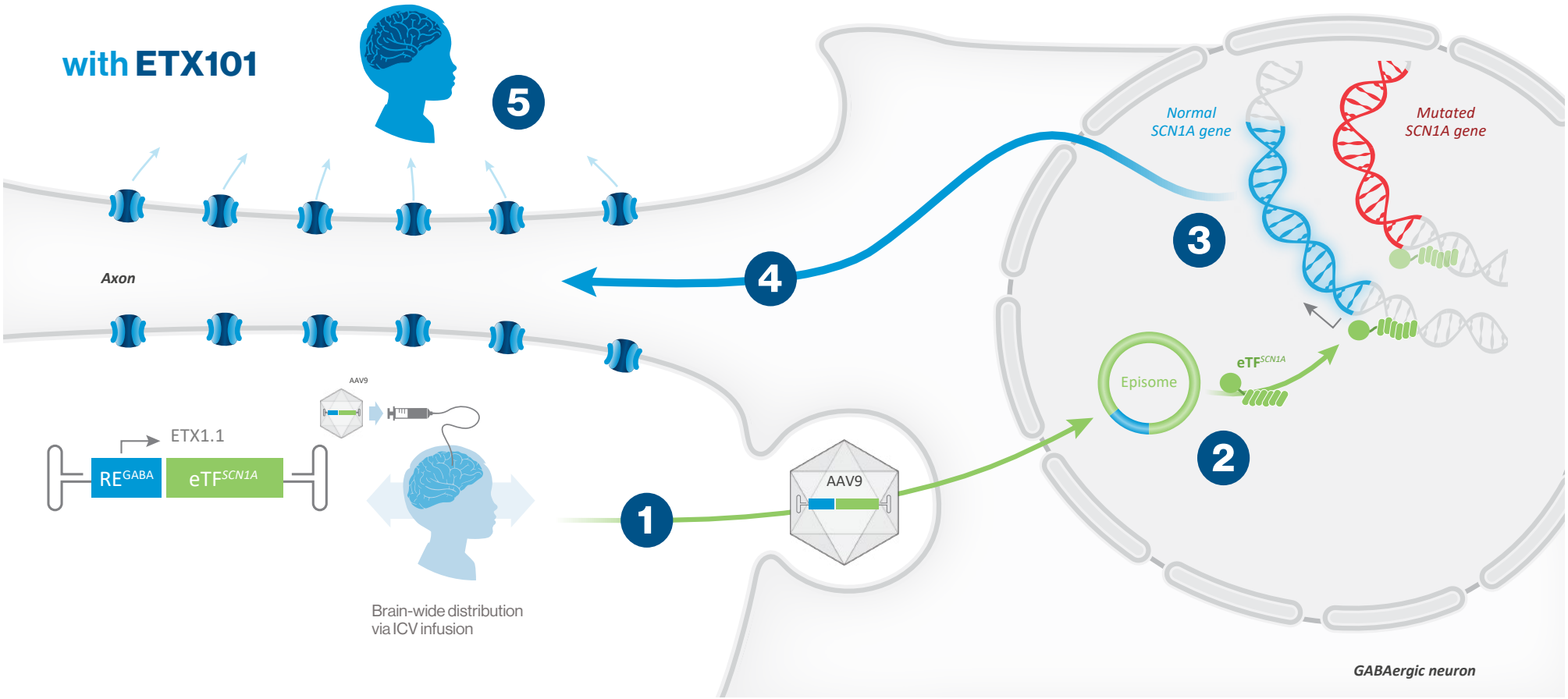
How ETX101 Works



1 AAV vector recognized by cell surface receptors and taken into neurons via endosome

2 Non-integrating therapeutic DNA delivered, forming double-stranded circular episome and initiating transcription under the regulation of the RE^{GABA} promoter to produce eTF^{SCN1A} in GABAergic neurons only

3 eTF binds to a specific sequence upstream of the transcription start site, resulting in increased SCN1A expression.

4 Increased SCN1A translation leads to increased density of NaV1.1 sodium channels.

5 Potential to address full range of disease manifestations by| precise upregulation of SCN1A expression within GABAergic inhibitory interneurons