
# AAV Manufacturing Considerations

**Annual bioProcessUK Conference**
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# NightstaRx Ltd – Formed in 2014

- Focused on development of AAV gene therapies for retinal dystrophies
- Backed by Syncona LLP (UK) and New Enterprise Associates, in the (USA)
- Based in London & Boston, a growing company, we outsource key activities
- Lead programme is gene therapy for Choroideremia, a rare inherited cause of blindness
- Moving into Phase III

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THE LANCET

Retinal gene therapy in patients with choroideremia: initial findings from a phase 1/2 clinical trial

Prof Robert E MacLaren, FRCOphth, Markus Groppe, PhD, Alun R Barnard, PhD, Charles L Cottriall, PhD, Tanya Tolmachova, PhD, Prof Len Seymour, PhD, K Reed Clark, PhD, Prof Matthew J During, FACP, Prof Frans P M Cremers, PhD, Prof Graeme C M Black, FRCOphth, Prof Andrew J Lotery, FRCOphth, Susan M Downes, FRCOphth, Prof Andrew R Webster, FRCOphth, Prof Miguel C Seabra, MD

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Gene therapy 'could be used to treat blindness'

By Pallab Ghosh
Science correspondent, BBC News

16 January 2014 | Health



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# Key AAV Manufacturing Challenges

1. **Scale up of laboratory process to industrial manufacture without compromising quality**

   Lab scale technologies can produce extremely pure and high quality AAV material but use cell culture and primary separation technologies which are a real challenge to scale (e.g. adherent cells, FBS, ultracentrifugation)

   Industrial processes meet yield and scale-up requirements but struggle to achieve the same quality (e.g. on 'full' DNA containing capsid content) or specific productivity (transfection efficiency etc.)

2. **Availability of qualified and truly quantitative assays and qualified reference standards or materials**

   Methods for determining AAV titre using quantitative PCR are assay protocol and standard dependent

   Infectious AAV titre assays are complex, multistage, indirect and highly variable

   Direct determination of full AAV capsid (AAV particles containing DNA) content of a batch is by techniques more suited to characterisation, rather than GMP product release testing (e.g. electron microscopy and analytical ultracentrifugation)

3. **Contract AAV GMP manufacturing capacity and experience**

   Later phase GMP manufacturing capacity and experience with AAV manufacture, testing and process validation requires development, especially in the UK


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