Manufacture of AVB-406, a BBB–crossing AAV vector for MAPT knockdown in Alzheimer's disease

Andrea Martorana, ASCGT, May 14th, 2026

Disclosure

- Andrea Martorana is an employee of AviadoBio Ltd and holds equity in the company. No other relevant financial relationships to disclose.

- AVB-406 is an investigational product and has not been approved by any regulatory authority

POWERED BY PRECISION™

AVB-406

AAV gene silencing *MAPT* to treat Alzheimer's disease and other tauopathies

TARGET

AVB-406 targets tau protein — the key driver of neuronal death and cognitive decline in Alzheimer's disease — with the goal of silencing it at the source before irreversible damage occurs.

PAYLOAD

A one-time RNA silencing platform engineered for best-in-class specificity, potency, and neuron-selective regulation.

vMiX™

DELIVERY

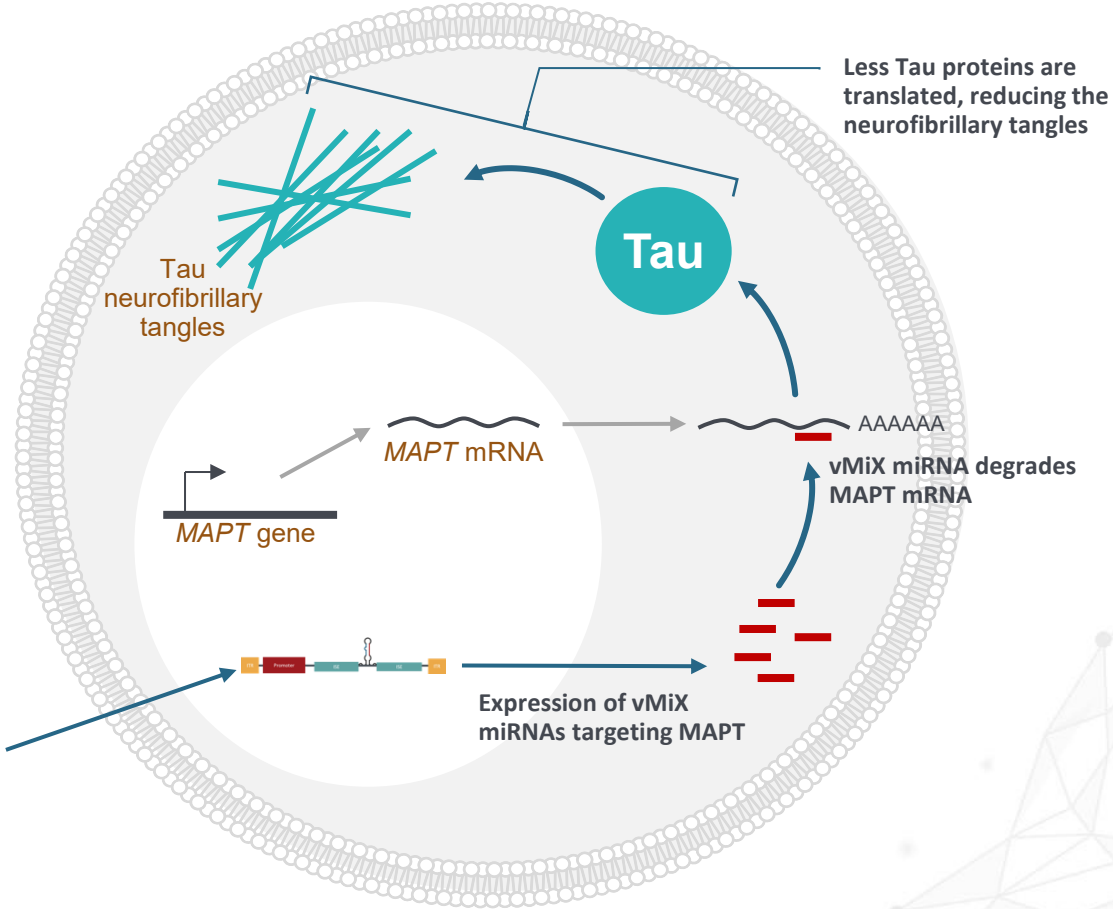
One-time IV dosing of a **novel capsid targeting TfR1**, supporting broad CNS biodistribution.

AVB-406 is being developed as a one-time, IV administered gene therapy to prevent and reverse Tau aggregation in tauopathies

Gene silencing payload with neuronal promoter

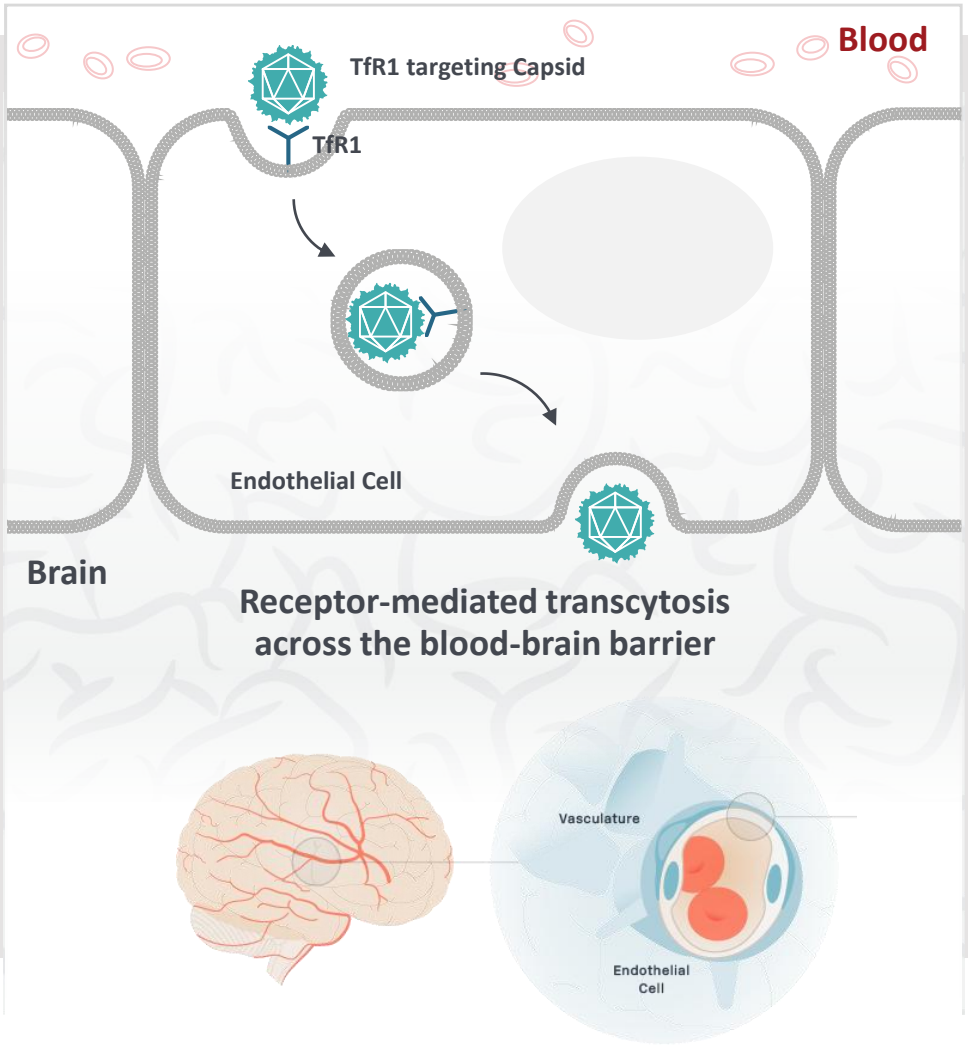
BBB-penetrant AAV capsid for systemic delivery

AVB-406 reduces Tau protein production via *Mapt* mRNA silencing, reducing neurofibrillary tangle formation



For further details on the development and translational validation of AVB-406 and vMiX™ refer to Abstract ID 354 by Romain Joubert

AVB-406 utilises a TfR1 capsid to enable selective CNS targeting



Benefits of AAV Targeting TfR1

- TfR1 is the **most extensively characterised BBB receptor** [1-3],
- **Clinically validated** [5].
- Rapid kinetics are **ideally suited for AAV gene therapy applications**[4]
- **Capsid binds exclusively to human form of TfR1**.
- Extensive biodistribution across CNS, with **up to 80% transduction across cortex** at low systemic doses and transduction of neurons and astrocytes
- Readily manufacturable. AAV9-like yields provides attractive CoGS

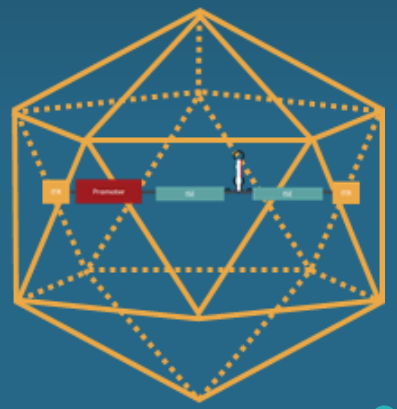
1) Bourassa, Mol Pharm. (2019);
2) Pardridge, Front Drug deliv. (2023);
3) Kumabe, Fluids and Barriers of the CNS (2025);
4) Pardridge, Pharmaceuticals (2021);
5) AVLAYAH FDA summary of prescribing information (2026)

AVB-406: From Manufacturing Excellence to CNS Efficacy

A BBB–crossing vector designed for CNS delivery

Recovery aligned with industry standards

AVB-406



Demonstrated manufacturability at scale with high purity and consistency

High purity and well-packaged DNA

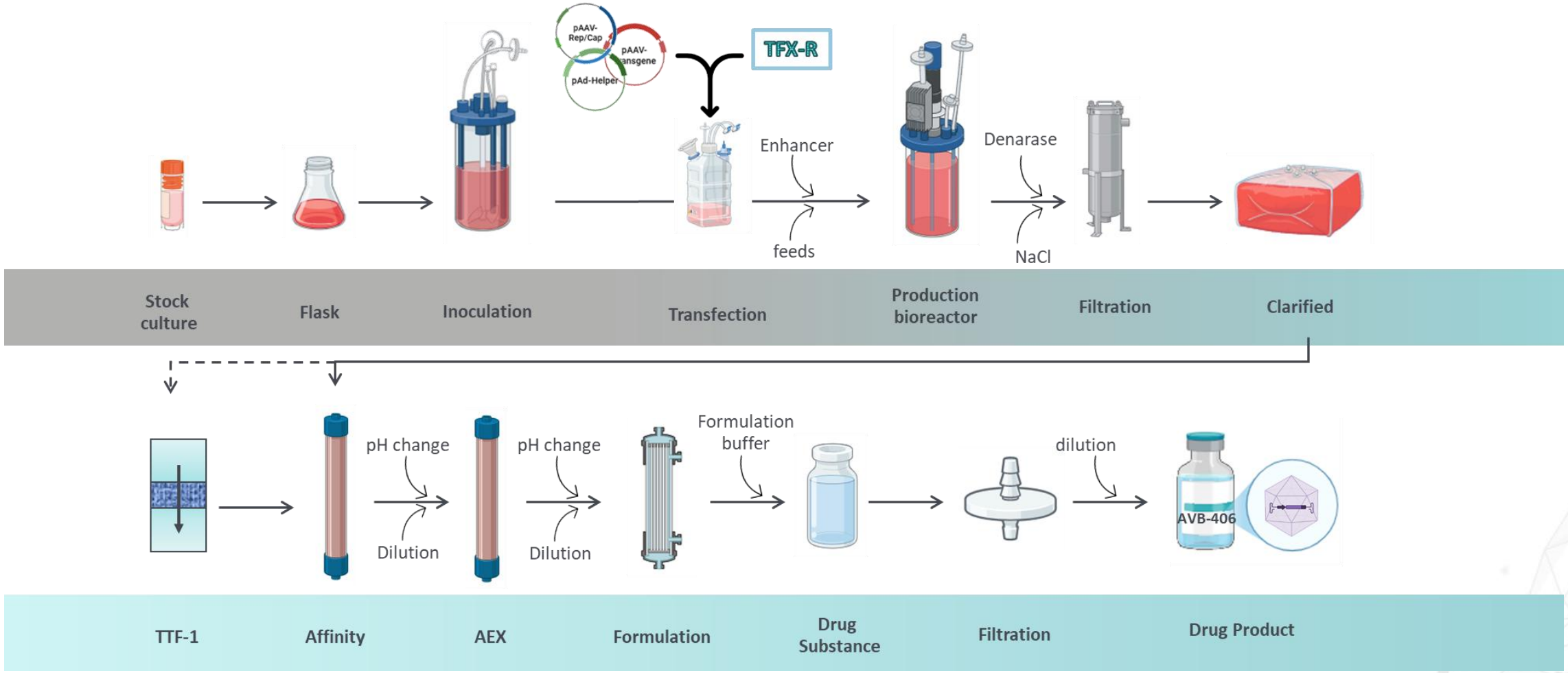
Chromatography based purification to allow scalability

Reduce MAPT gene expression in a dose-dependent manner in cell-based assays

Reduce MAPT mRNA in brain, cortex and hippocampus*

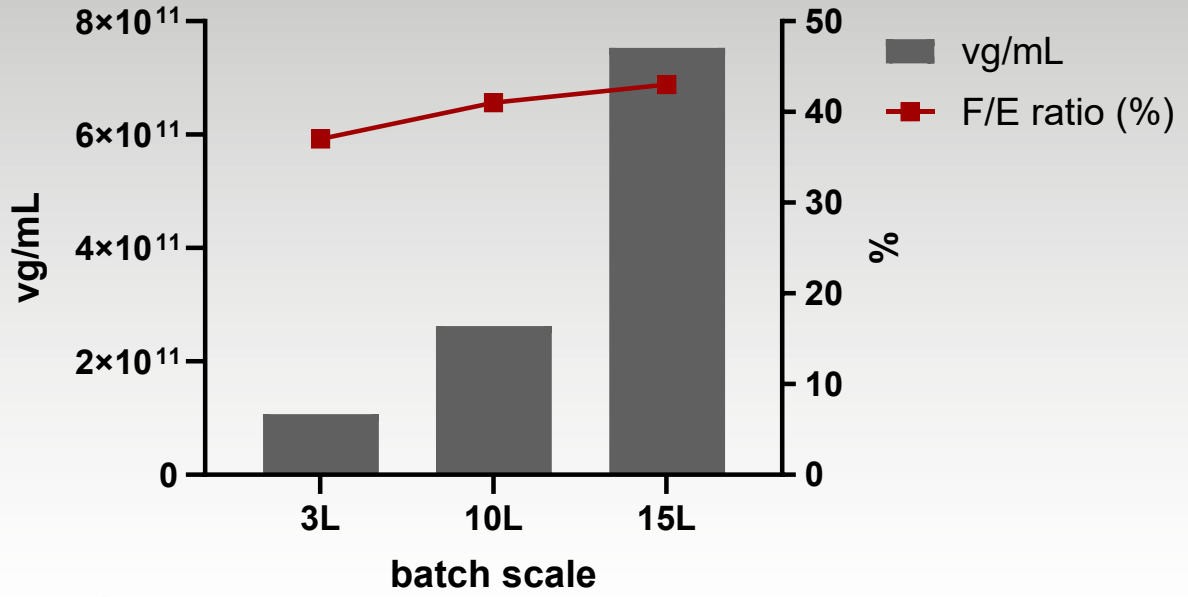
For the preclinical development of AVB-406 refer to Abstract ID 234 by Carlos Miranda

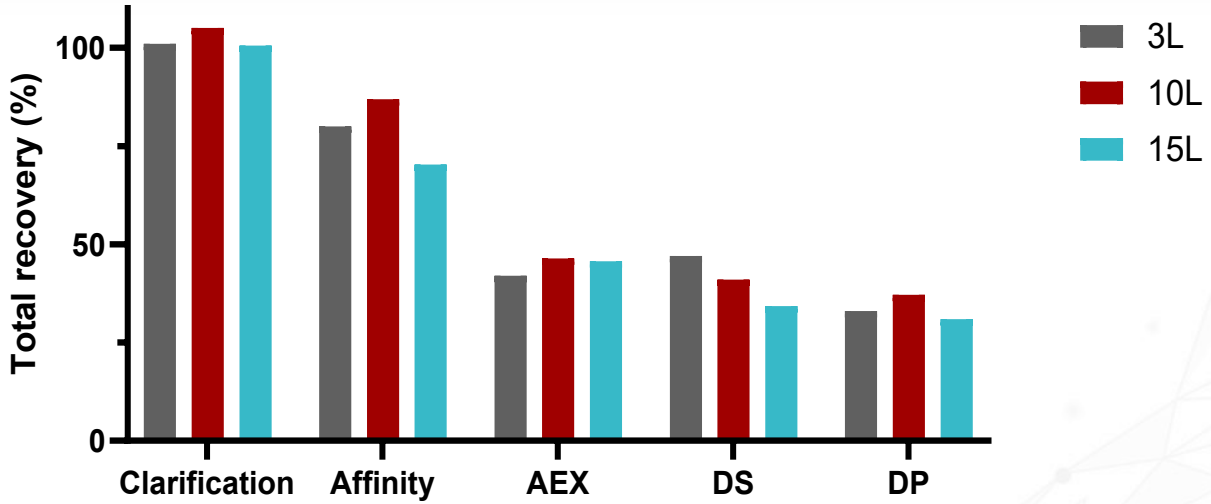
Process manufacture of AVB-406



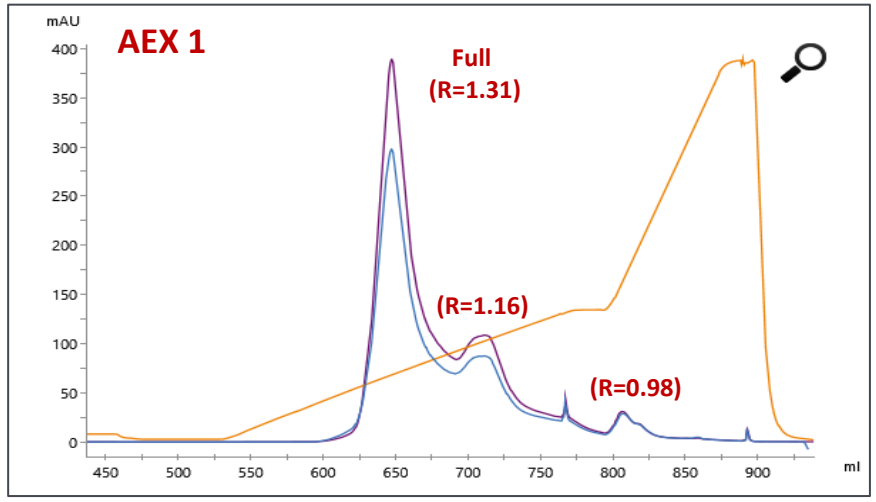
Productivity at scale

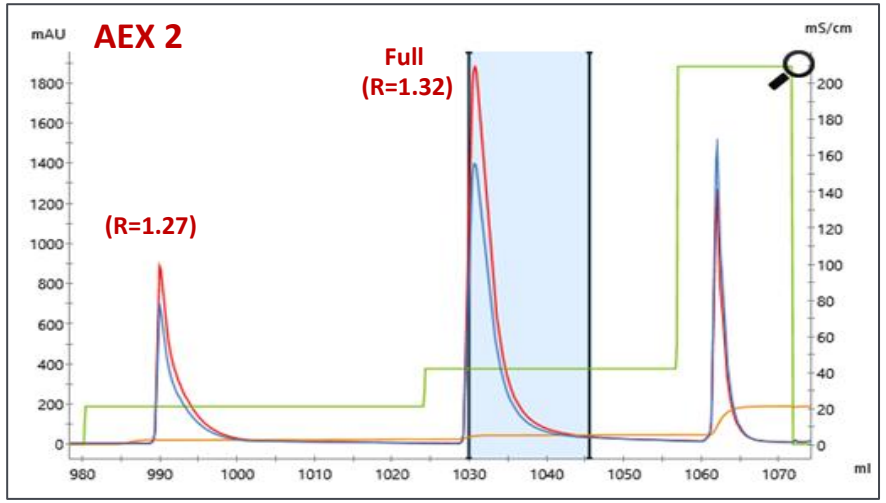
- ❑ Productivity increases with the scale
- ❑ Process successfully replicated by CDMO doubling productivity
- ❑ Yield exceeded 30% regardless of the scale
- ❑ AEX and formulation are the bottleneck of the process

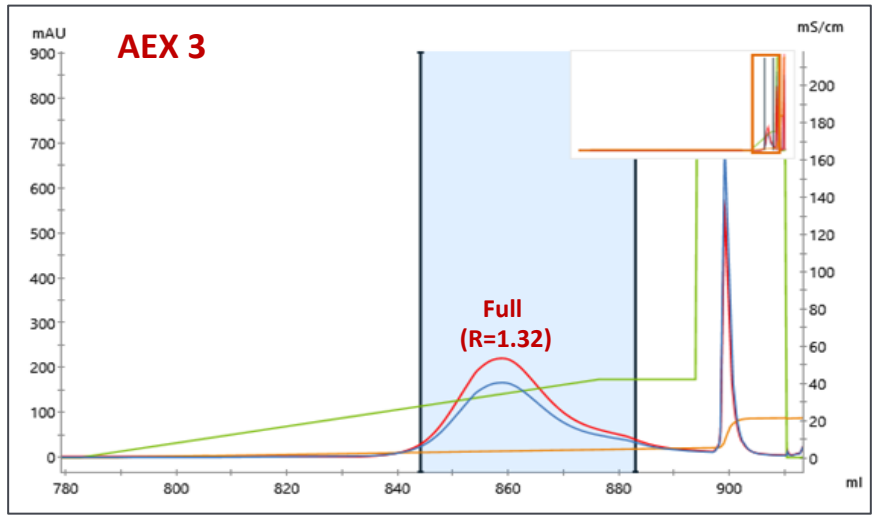


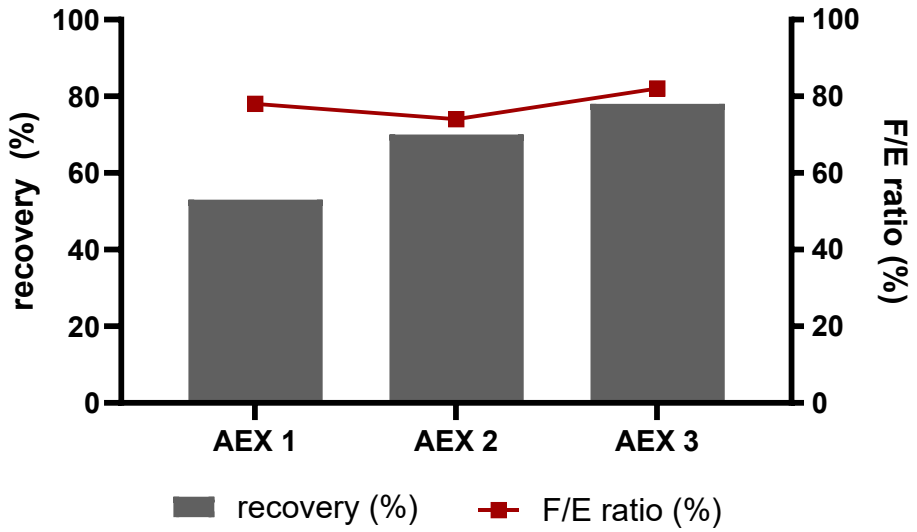


Optimising AEX recovery through tailored gradient conditions









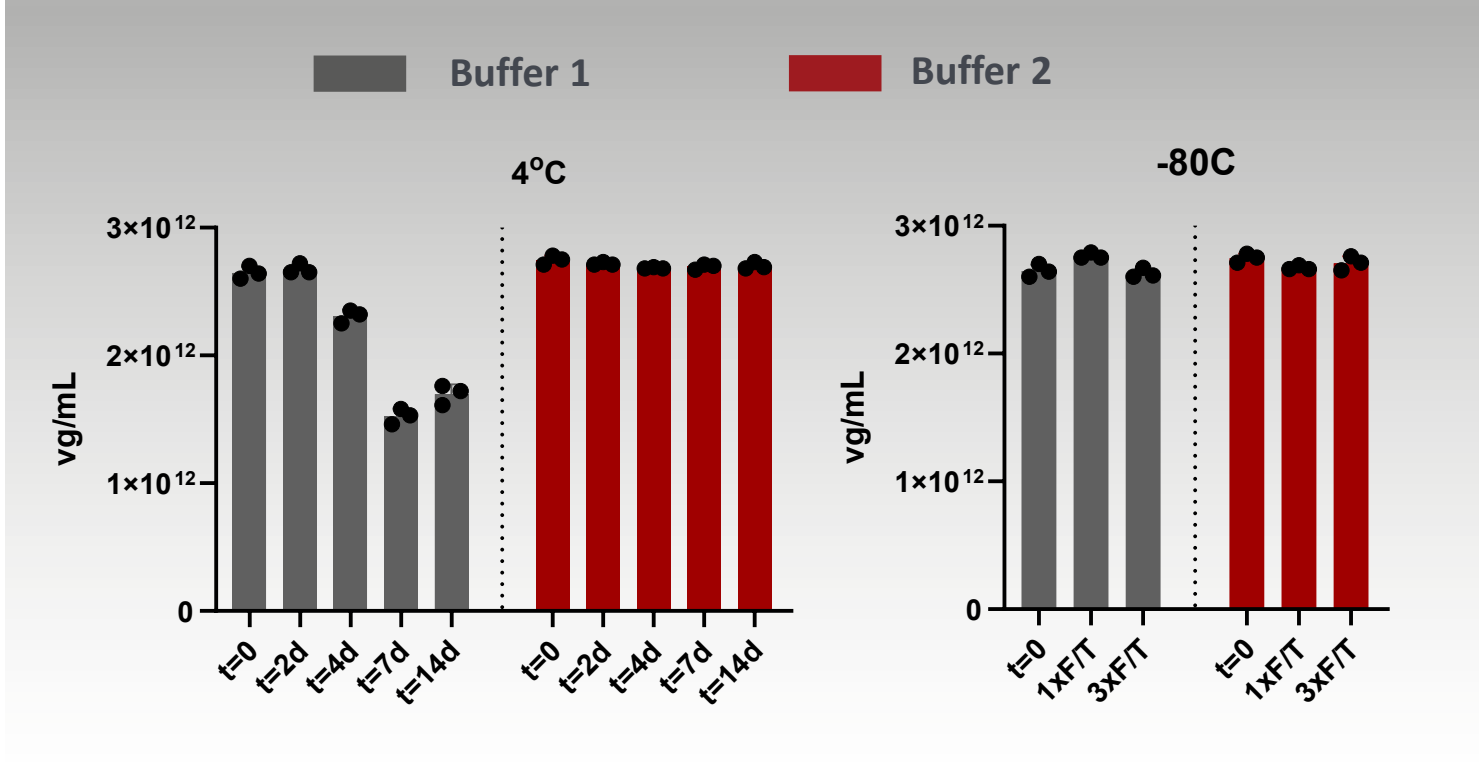
Enrichment performance in AEX is product-dependent

- Heterogeneity of the sample makes separation challenging
- Co-elution of empty and full capsids may affect recovery
- Converting step into linear gradient can increase recovery

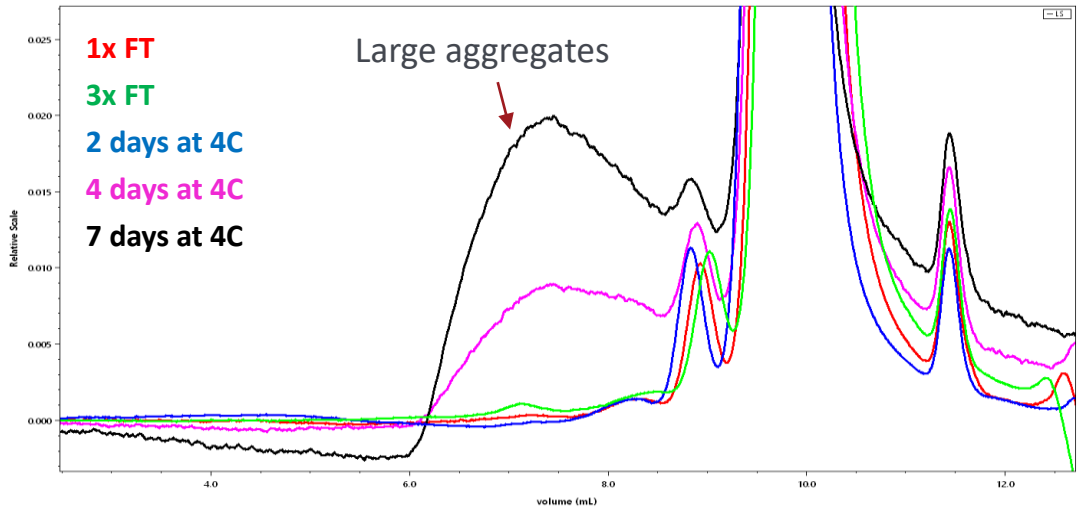
Critical parameters in formulation and stability

Lessons learnt

- Small modifications on the capsid may promote aggregation
  - Optimize shear stress rate and buffer composition
- Consider buffer exchanging at low concentrations
- Buffer composition may influence stability at 4-8ºC
- Freeze/thaw cycles have often no impact on DS titre or quality



SEC-MALS traces of AVB-406 in FB1



PURITY

99% purity

VP1:VP2:VP3 ratio of 4.5/1.2/1

>85% full particles

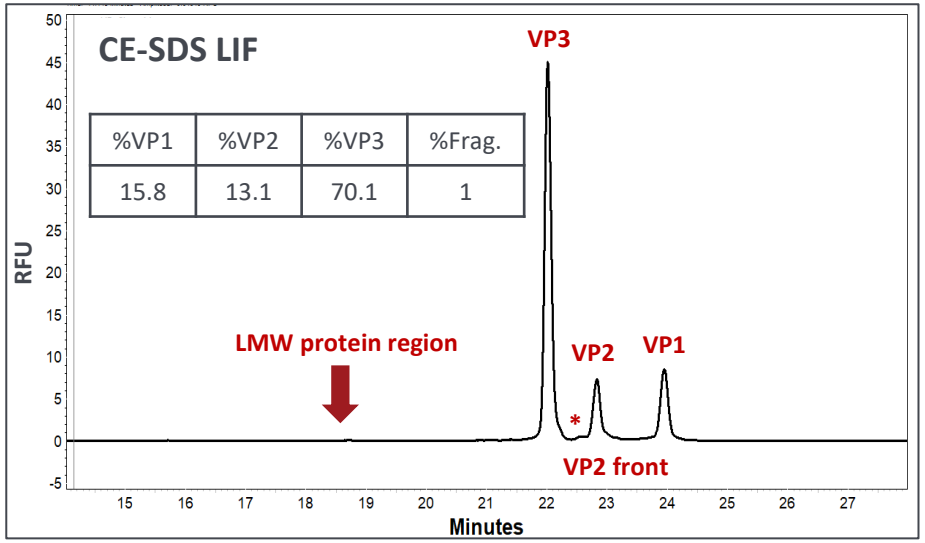
QUALITY

<5% aggregation by SEC-MALS

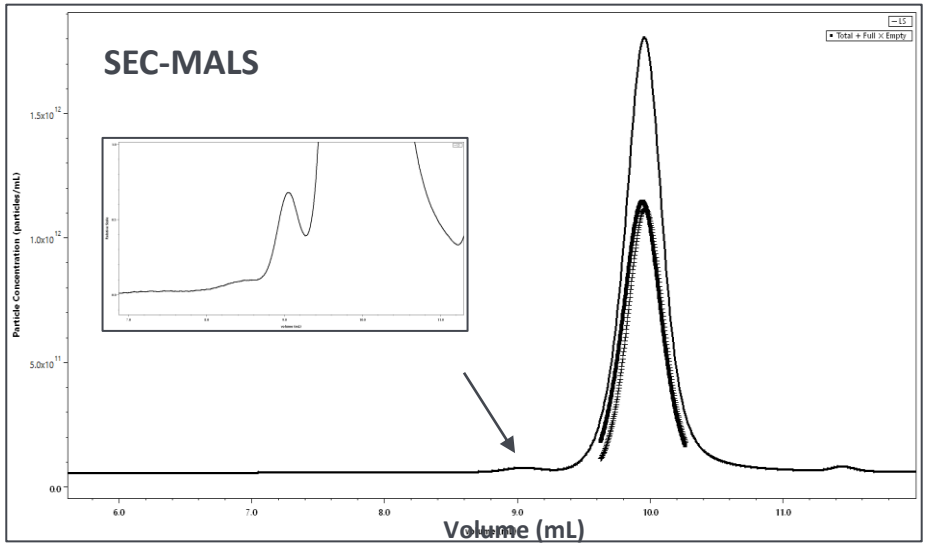
>40% main genome by CE-GI

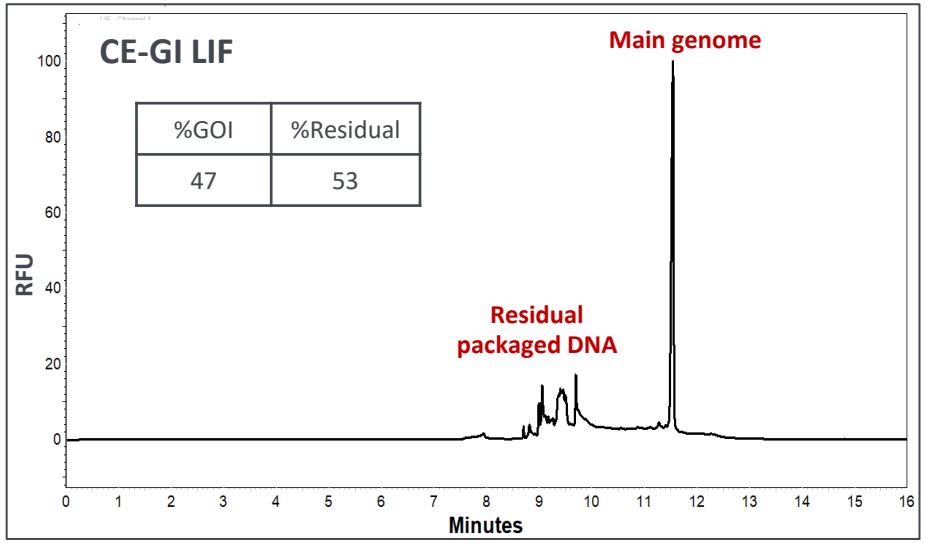
POTENCY

Consistent knockdown with 3 MOIs in the linear range

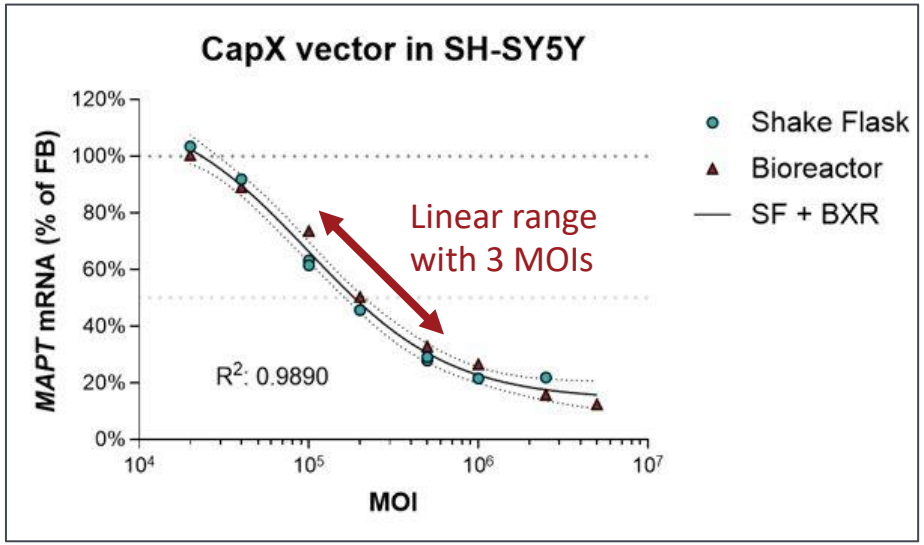


%VP1	%VP2	%VP3	%Frag.
15.8	13.1	70.1	1





%GOI	%Residual
47	53



AVB • 406

for Alzheimer's Disease
and other tauopathies

AVB-406 is positioned for clinical study initiation in 2026

ACHIEVEMENTS

- A scalable, chromatography-based purification process was developed for AVB-406
- Manufacture was successfully transferred to CDMO with high productivity
- High purity with high-quality packaged DNA
- Recovery in line with industry standards

MILESTONES

- ✓ vMiX miRNA lead candidate selected
- ✓ IV BBB-crossing capsid selected
- ✓ Proof-of-mechanism (PoM) and Proof-of-concept (PoC) in mouse
- ✓ GLP tox initiation in 2Q26
- ❑ Clinical study initiation 4Q26

Acknowledgments

AVIADOBIO

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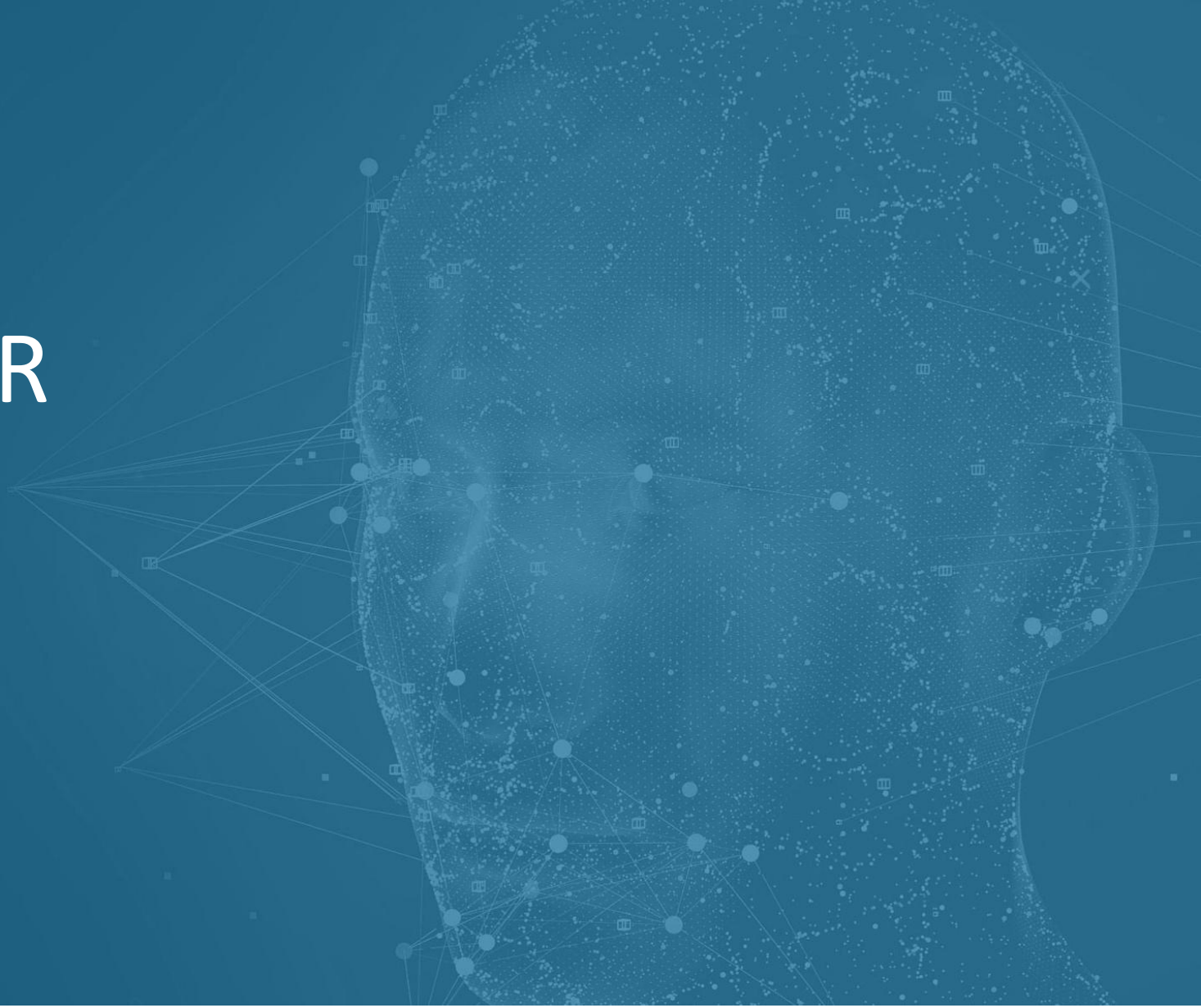

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