Manufacture Of AVB-406, A BBB-Crossing AAV Vector For MAPT Knockdown In Alzheimer's Disease

Cell 2026

- Michael MacDonald

AviadoBio: We are delivering the future of gene therapy



MISSION & TEAM

Relentlessly chase cures by translating groundbreaking science and precision delivery into life-changing medicines. UK-based, globally focused with a highly experienced team of 50+.



FOCUS

AVB harnesses precision genetic medicine to restore and protect neuronal function across the central nervous system.

Our focus is on targeted gene therapy delivery and precise dosing to maximise biodistribution to neuronal tissue with a favourable safety profile.

This is enabled by our core expertise in targeted delivery, potent genetic payloads, and rapid translation.



STRATEGY

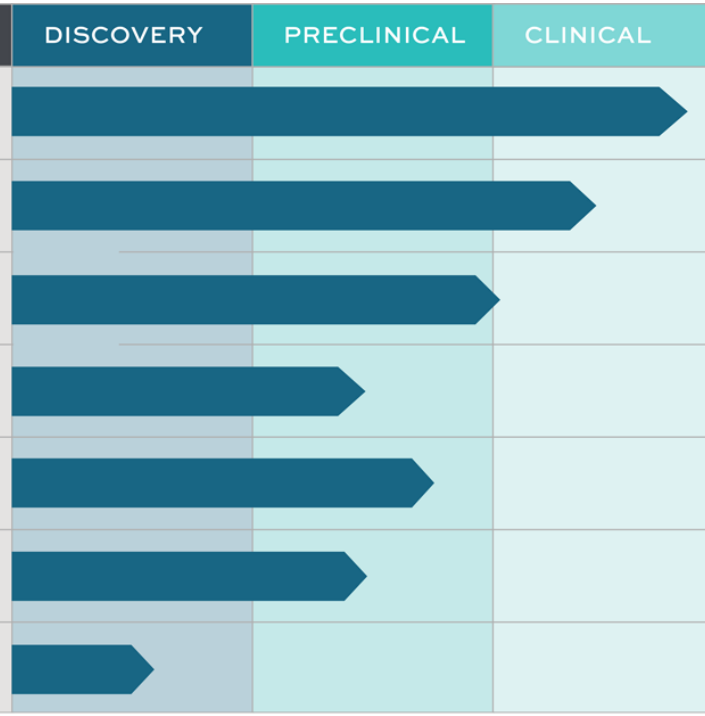
A hybrid approach allows us to advance our pipeline on multiple fronts by leveraging internal skillsets balanced with external niches.

Clinical trials in the UK, EU, US, and China.

Multiple programs with a mix of internal and external roles.

FOCUSED ON ADVANCING A PIPELINE OF TARGETED GENE THERAPIES

PROGRAM	TARGET	PAYLOAD	DELIVERY	INDICATION	PARTNER
AVB-101	GRN	Gene supplementation	ITM	FTD-GRN	Wholly owned
AVB-307*	Novel Opsin	Optogenetics	IVT	Retinitis Pigmentosa	UgeneX 星明优健 (China only)
			IVT	Geographic Atrophy	
			IVT	Other Retinal Dystrophies	
AVB-406	MAPT	vMiX™ RNA silencing	IV	AD & Other Tauopathies	Wholly owned
AVB-203	SOD1	vMiX™ RNA silencing	IV	ALS	Wholly owned
Undisclosed	Undisclosed	vMiX™ RNA silencing	Undisclosed	Undisclosed	Wholly owned



GRN, Progranulin, MAPT, Microtubule-associated protein tau. AD, Alzheimer's Disease. ALS, amyotrophic lateral sclerosis. ITM, intrathalamic. IVT, intravitreal. IV, intravenous.
*AVB has the exclusive option to license AVB-307 (UGX-202) for all human uses outside China

vMiX is AviadoBio's proprietary vectorized RNAi platform



PROMOTER

Pol II-based design enables tissue/cell specific promoter usage to control expression profile improving targeting and safety.

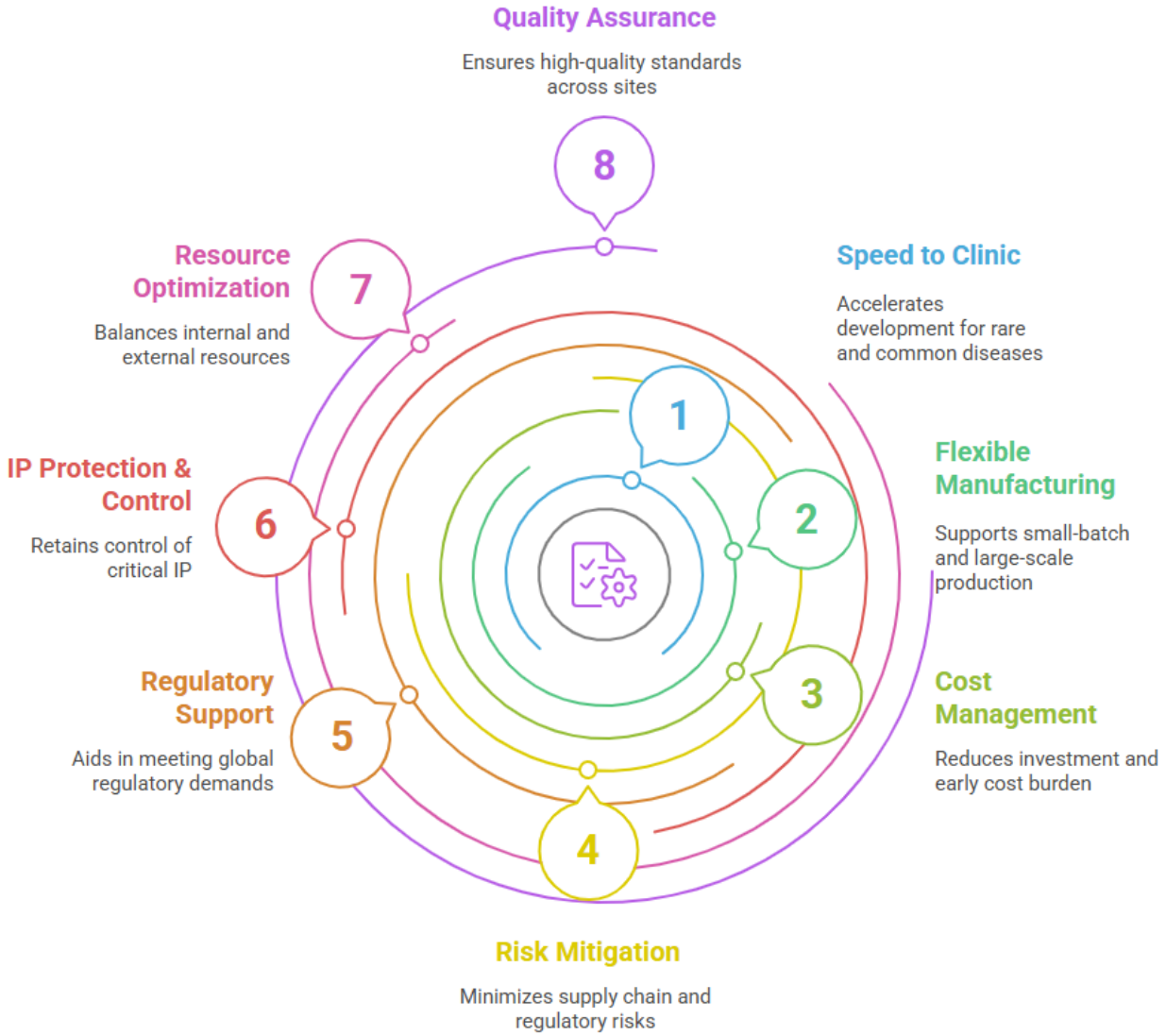
THERAPEUTIC PAYLOAD

miRNA delivery using unique hybrid hairpin design, with potential to deliver multiple miRNAs

Flexible design allows inclusion of coding cDNA for 'Replace & Silence' strategies

- ☑ Efficient silencing of gene targets
- ☑ Excellent fidelity miRNA production
- ☑ High translatability from *in vitro* to *in vivo*
- ☑ Highly manufacturable in AAV

The Hybrid Model: Underlying Theory



The Hybrid Model: A case study of AVB-406*

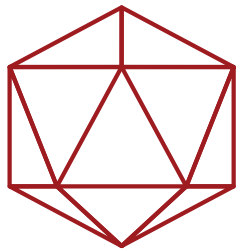


50 people

- *25 in TechOps*
- *13 in CMC*
- *6 in PD*

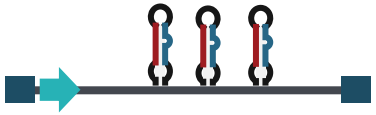
**Note: AVB-406 is in development and not yet approved by any regulatory authority.*

The Hybrid Model: A case study of AVB-406



AAV9

+



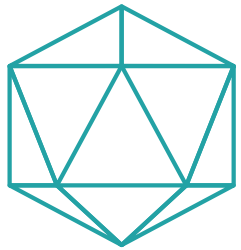
Internal IP
(vMiX™ payload)

AVIADOBIO

Proof of concept:

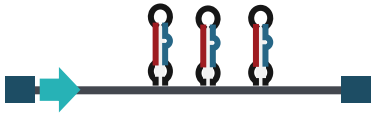
- *Develop USP V1.0*
- *Develop DSP V1.0*
- *Develop analytics V1.0*

The Hybrid Model: A case study of AVB-406



Novel Capsid

+



Licensed IP
(Capsid)

Internal IP
(vMiX™ payload)

AVIADOBIO

Proof of concept:

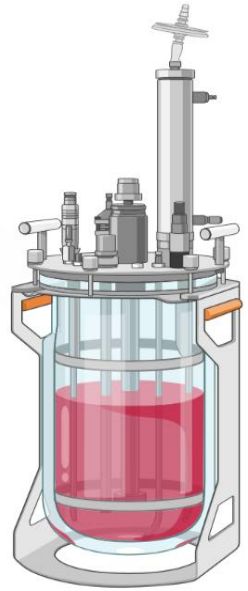
- *Develop USP V2.0*
- *Develop DSP V2.0*
- *Develop analytics V2.0*

The Hybrid Model: A case study

Collaborations
(Industry, academia)

Licensed IP
(Capsid)

Internal IP
(vMiX™ payload)



Bioreactors

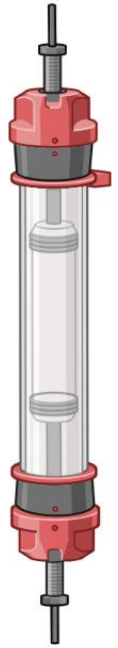


Cell Lines

AVIADOBIO

Develop scalable process:

- *Develop USP V3.0*
- *Develop DSP V3.0*
- *Develop analytics V3.0*



Chromatography resins



Buffers

The Hybrid Model: A case study

Collaborations
(Industry, academia)

Licensed IP
(Capsid)

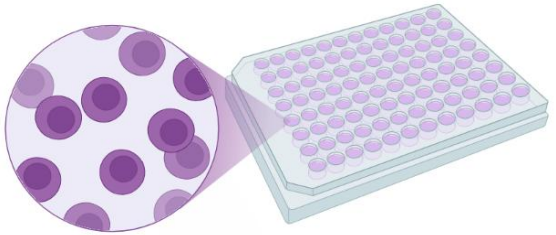
Internal IP
(vMiX™ payload)

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GLP batch:

- *Establish functionality.*
- *Identify process issues.*

Animal Studies
(Tox, POC)



Potency assays



Mouse studies

The Hybrid Model: A case study

Collaborations
(Industry, academia)

Licensed IP
(Capsid)

Internal IP
(vMiX™ payload)

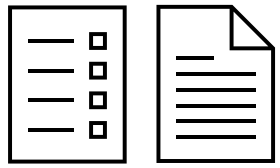
AVIADOBIO

Animal Studies
(Tox, POC)

CDMO
(Tox, GMP)

GMP production:

- *Supply chains.*
- *Scale and practicality.*
- *Tech transfer.*

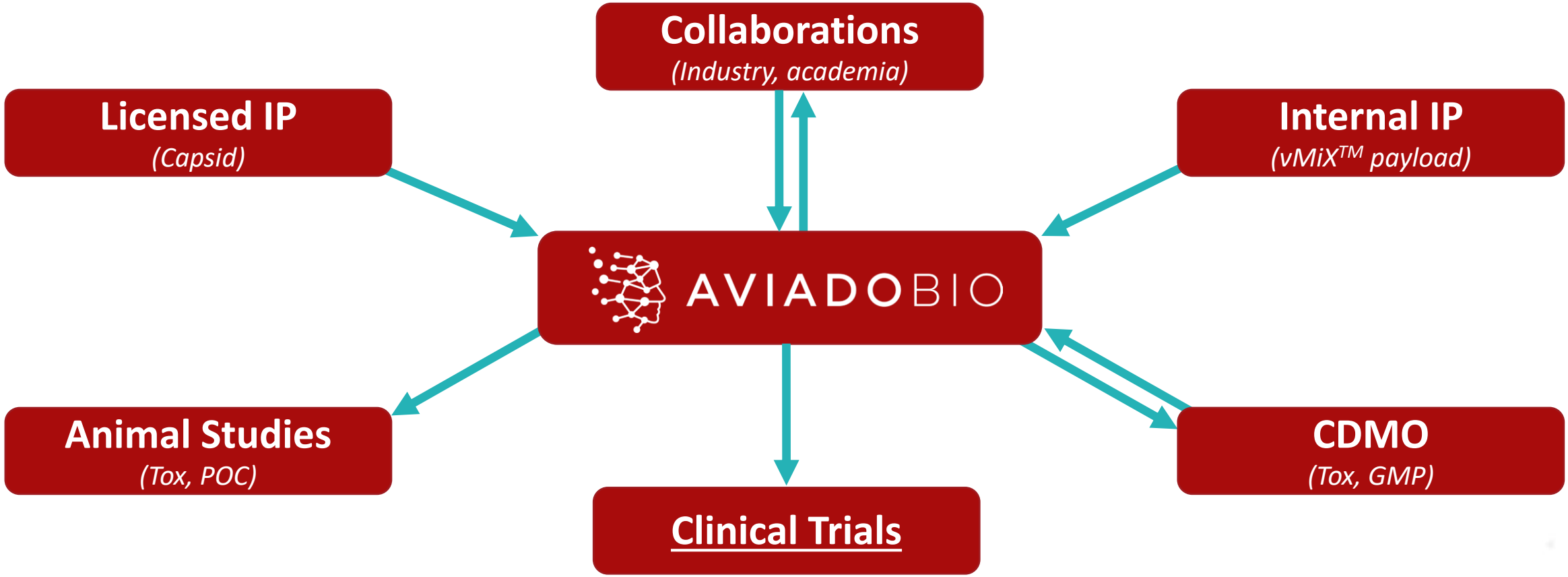


Documentation, regulation



Scaled production

The Hybrid Model: A case study



Upstream development challenges

V1.0 Process:

- 1E10 VG/mL
- <20% full particles

Challenges

Hybrid Process Development

- Cell line
- Feeds
- Plasmid ratios
- Transfection reagent
- Transfection reagent ratios
- Cell density

Outcomes

V3.0 Process:

- 2E11 VG/mL
- 40% full particles

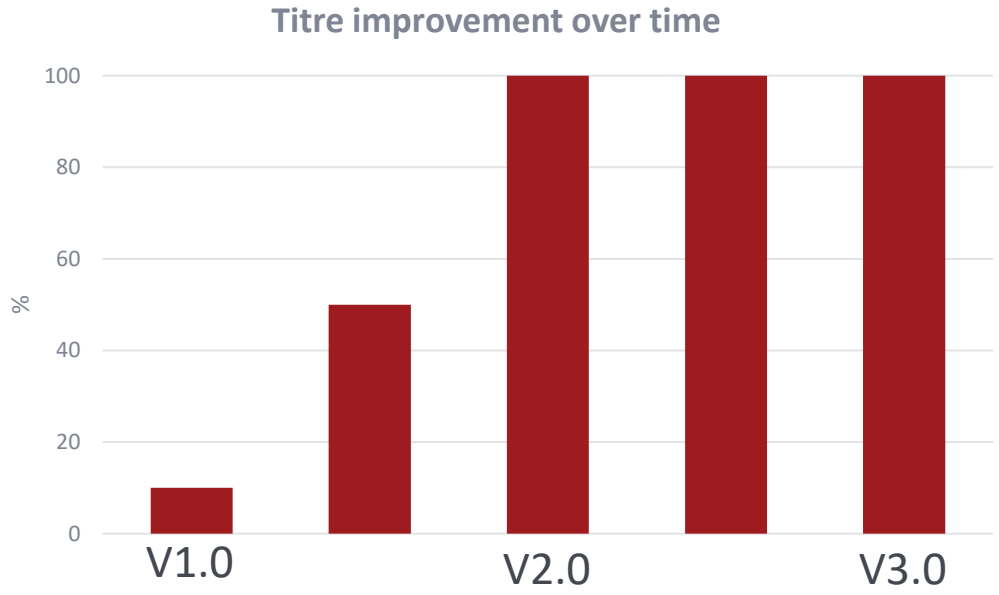
Upstream development challenges: Example

Initial OFAT experiments yielded promising results:

- Cell culture medium
- Feeds
- Transfection reagent

A ceiling was reached at 2E12 VG/mL.

- 1E6-5E6 Cells/mL → minor variations in titre.
- 0.8-2.0 ug DNA/E6 cells → minor variations in titre.



Pivot to increase in full particle %.

- Lower values reduced medium consumption, growth time, plasmid quantity.
- Lower values also increased % full by two-fold.

Downstream development challenges

V1.0 Process:

- 6E12VG/mL max.
- 22% recovery
- 3 days @ 4ºC

Challenges

Hybrid Process Development

- Affinity buffers and method.
- AEX resin.
- AEX buffers and method.
- Formulation buffers.
- UD/DF method.
- Formulation buffers (again).

Outcomes

V3.0 Process:

- >6E13 VG/mL
- 35% recovery
- >14 days @ 4ºC

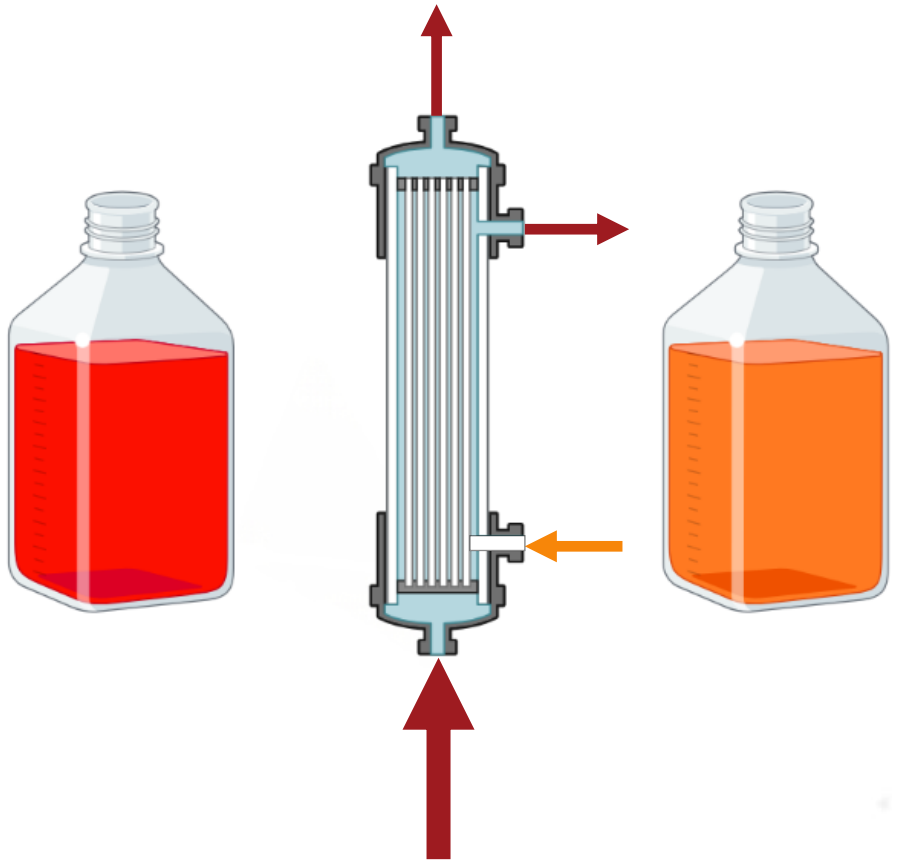
Downstream development challenges: Example

During production, the capsid aggregates at UF/DF.

Tests performed to adjust:

- Shear stress (flow rate, diameter).
- Concentration (at diafiltration stage).
- Formulation buffer.
- Membrane area.

Combined alterations in buffer and UF/DF method simultaneously eliminated aggregation and improved stability.

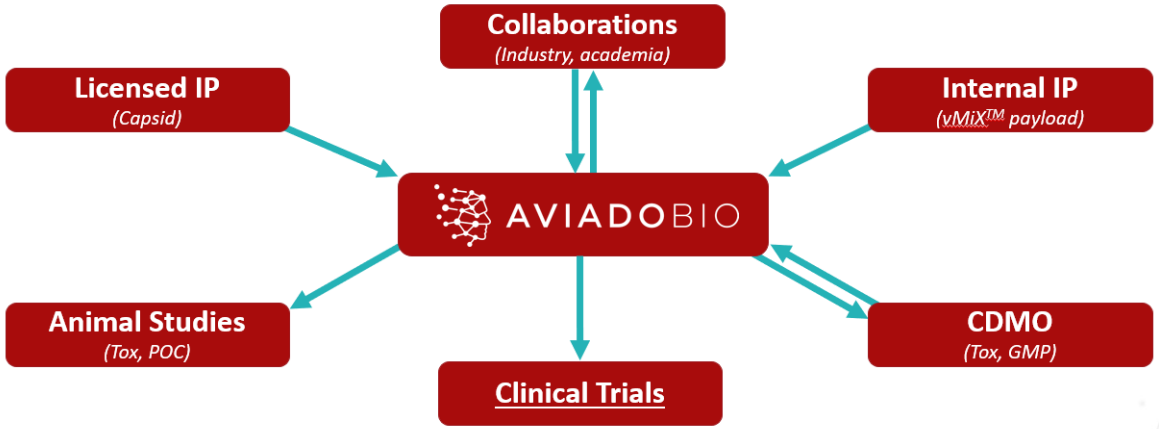


Conclusion

The development of AVB-406 was accomplished through a hybrid approach:

- Internal and external expertise supported AVB-406 process development.
- Progress reveals new challenges and solutions.
- Challenges can be solved iteratively and collaboratively.
- Connecting specialised teams and services accelerates outcomes.
- Results are transferrable and relationships are established.





Acknowledgements

Thanks to the team at AviadoBio, especially Process Development:

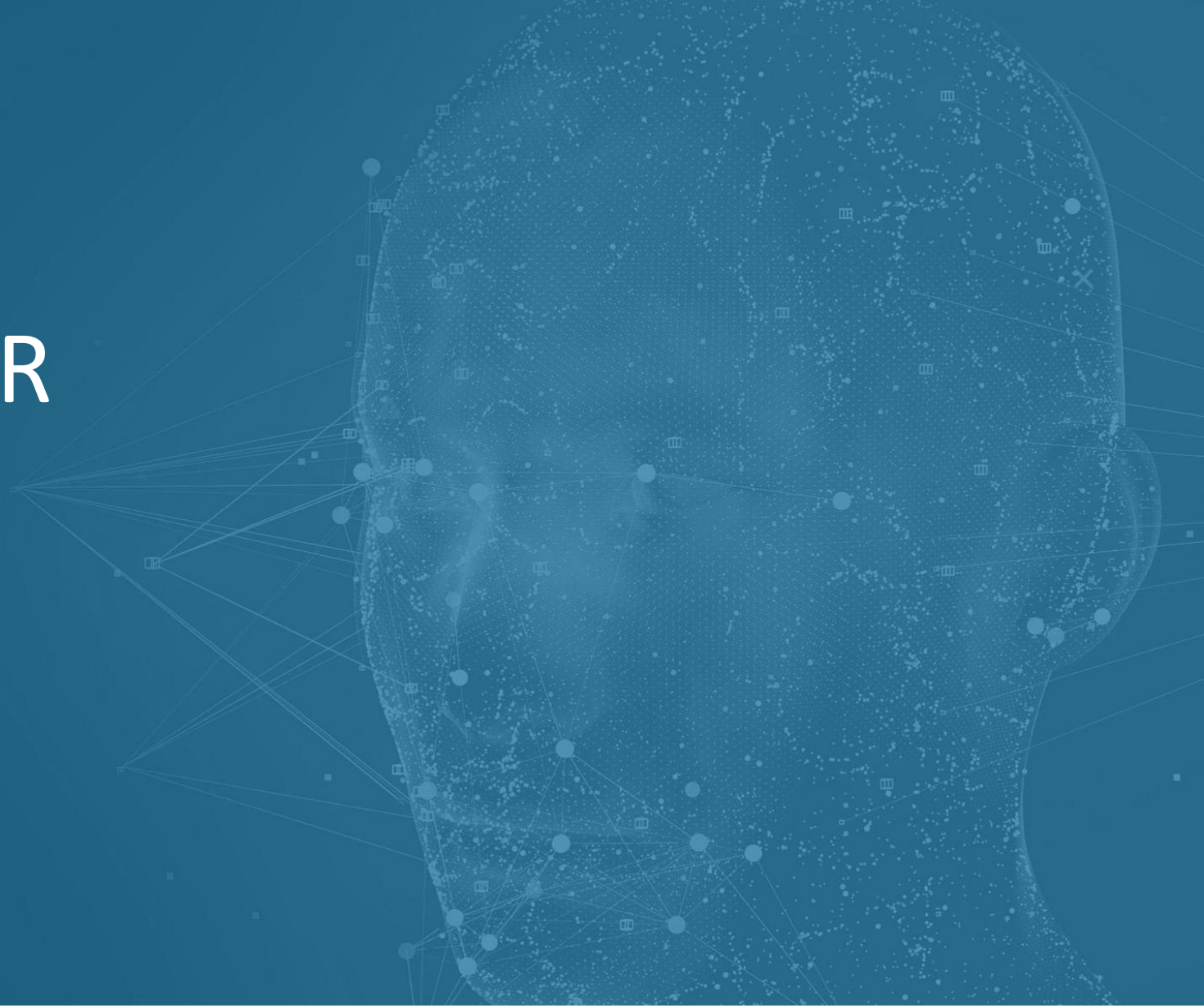
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- Megan Donnelly
- Alex Foster
- Andrea Martorana

THANK YOU FOR YOUR TIME

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