A proprietary HEK293 AAV production system can achieve greater than 50% full capsids with greater than 1e15vg/L at harvest enabling scalable chromatography-based polishing with high yield and purity

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Fulfilling the promise of gene therapy via targeted delivery

Best-in-class cardiotropic and BBB-penetrant capsids

- Cardiotropic capsids: 90% transduction of cardiomyocytes in NHP and de-targeting liver and DRG, with applicability to genetic cardiomyopathies
- BBB-penetrant capsids: Transduction of >50% neurons across spinal cord, cortical, and deep brain regions while de-targeting liver and DRG with applicability to multiple CNS diseases

Industry-leading delivery platform

- ART: **A**ffinia **R**ationally-designed **T**herapies applying structure modeling and regressive and generative ML/AI
- Multi-parametric selection based on tropism, manufacturability, immune-phenotype, and translatability
- Potentially applicable to non-AAV modalities

Early focus on manufacturability

- Screen for highly productive capsids
- Comparative manufacturability studies during lead identification
- Evaluation of emerging technologies and manufacturing innovation
- We have achieved yields over 3e15 vg/L with 40% full capsids at harvest

BBB: Blood brain barrier
ML/AI: Machine Learning/Artificial Intelligence

Yield and polishing are the two most important areas of focus in AAV process development

500L Bioreactor

Standard upstream process

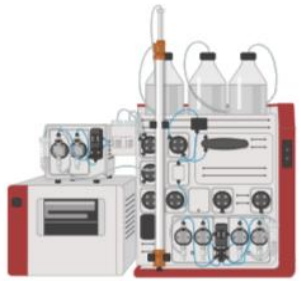
1.5e17 total vg
(3e14 vg/L)

>6e16 total vg purified
(40% process recovery)

25 doses
(2.4e15 total dose*)

Need to improve yields
Need to improve % full capsids

OR



Standard polishing process

85-95% full
~80% step yield

50-70% full
~60% step yield

Need to improve AEX yields and enrichment

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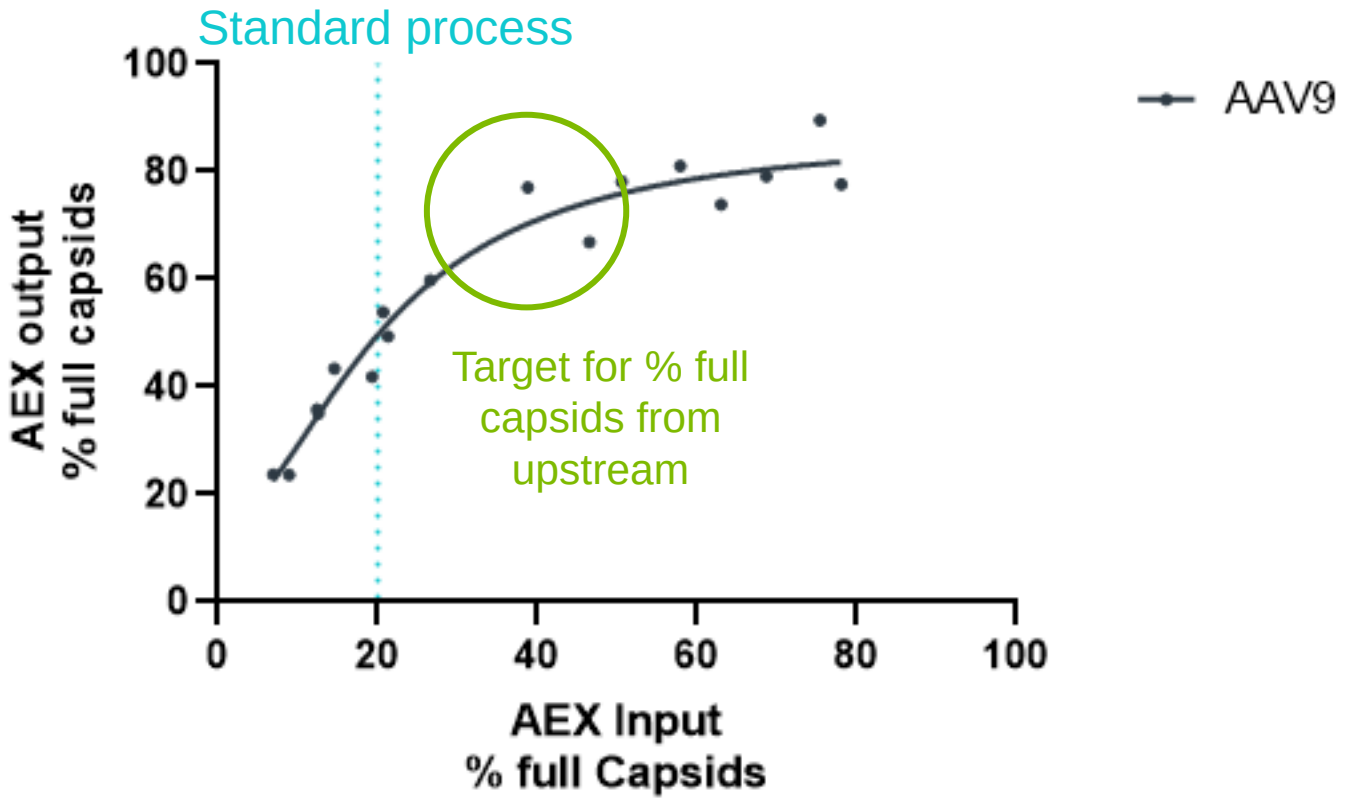
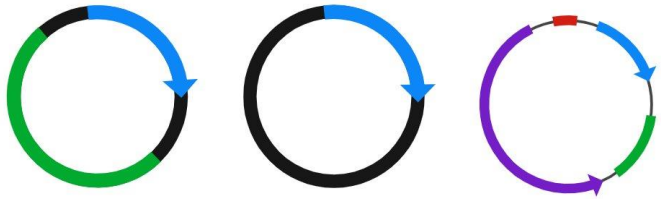
*Assumes 80kg patient at 3e13 vg/kg

Upstream productivity directly affects AEX effectiveness

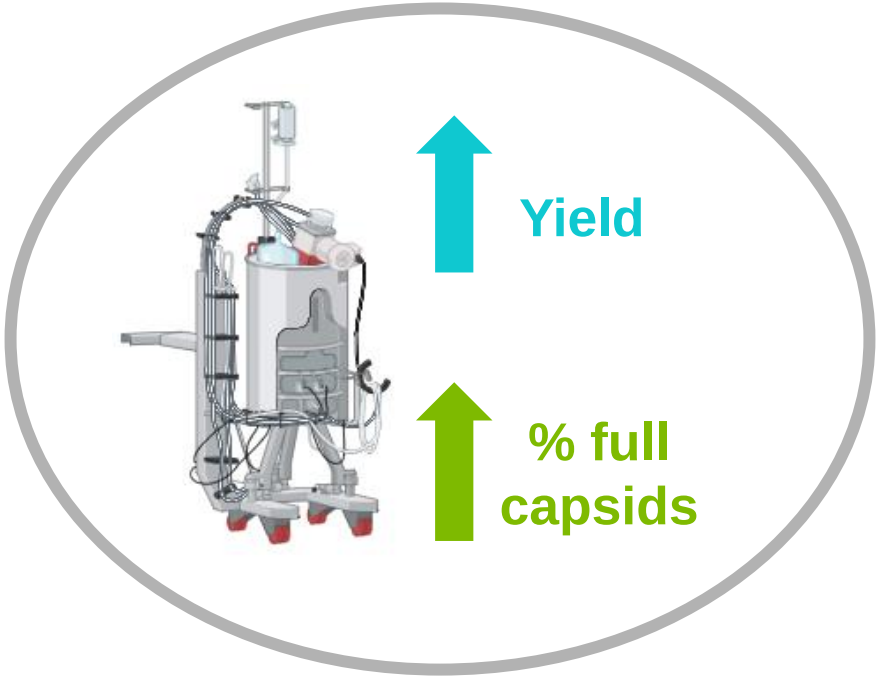


>40% full capsids at upstream are needed to reach highest percent full in BDS with high step yield

There are many ways to improve upstream yields and % full capsids



Plasmid design



Cell line optimization

Media optimization

Transfection reagent / other additives

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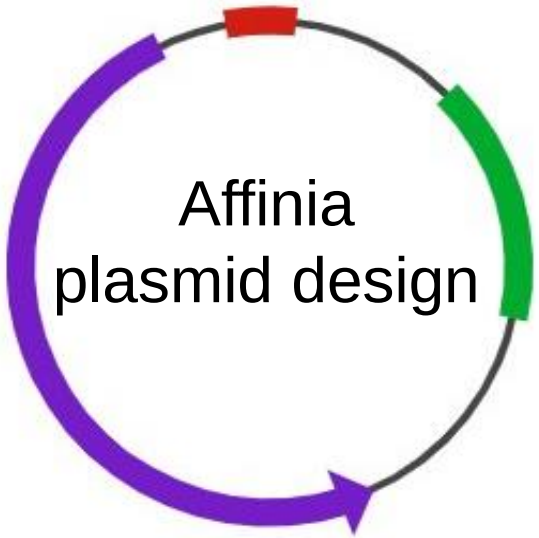
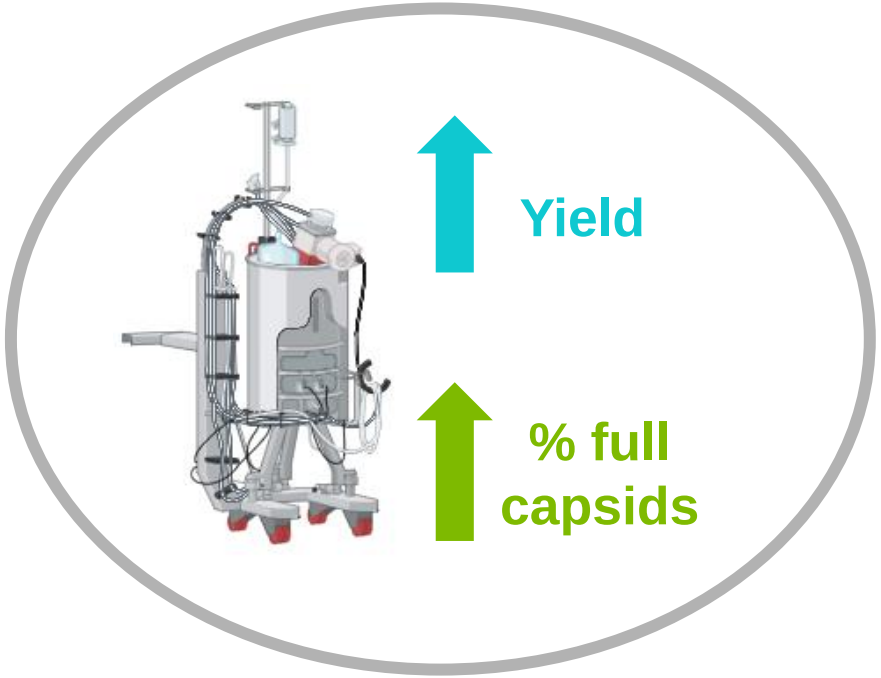
Affinia plasmid design results in significant improvement in upstream performance





Plasmid design works across:

- Serotypes
- Transgenes
- Transgene sizes
- Scales

Our plasmid design is readily implemented into any HEK293 suspension process

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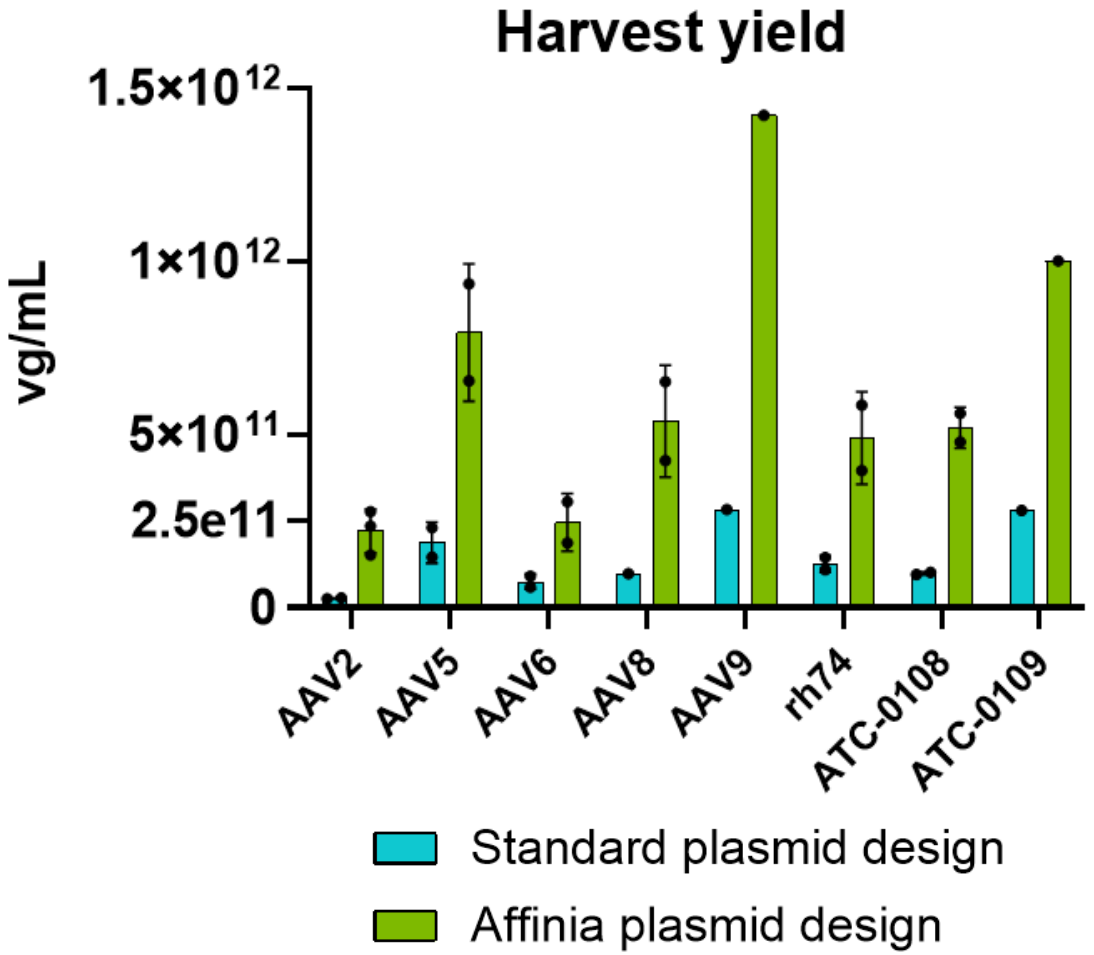
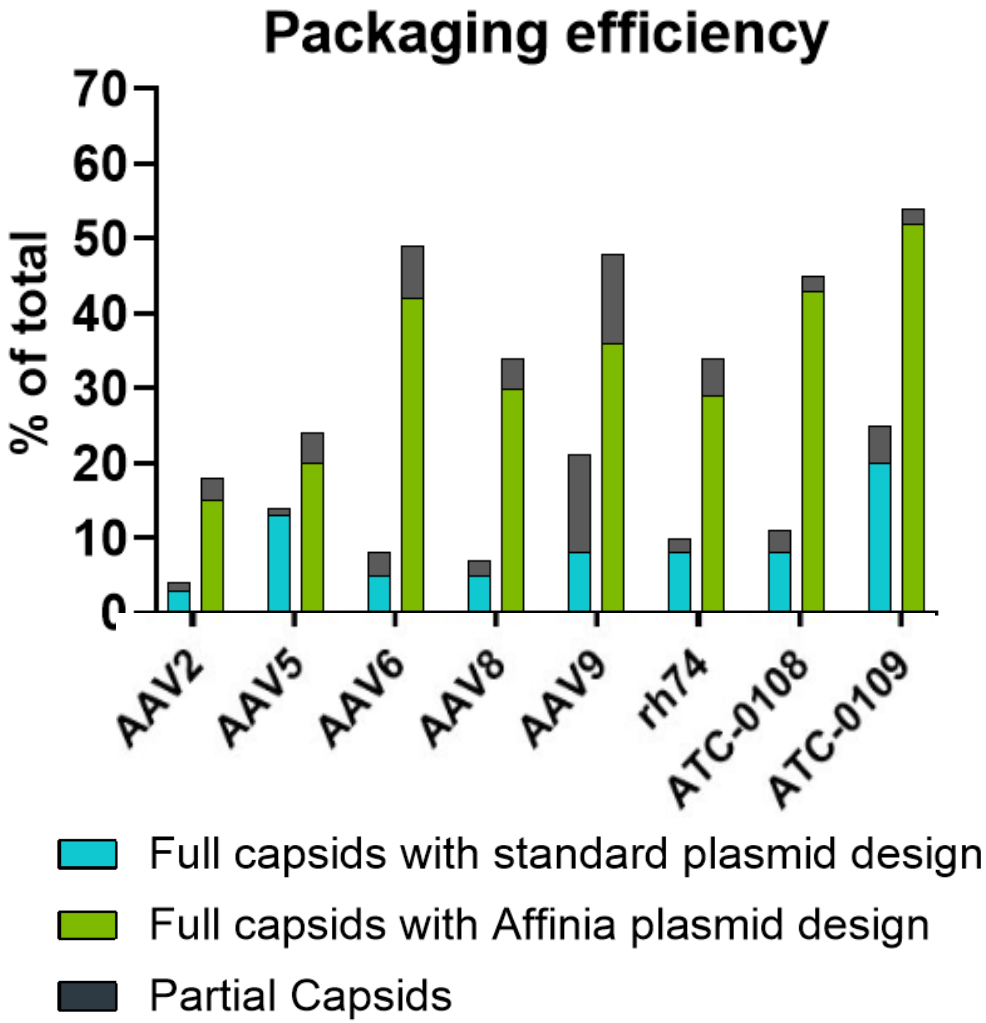
Affinia plasmid design improves yields 3-7x and improves % full capsids 2-4x for multiple WT and novel serotypes

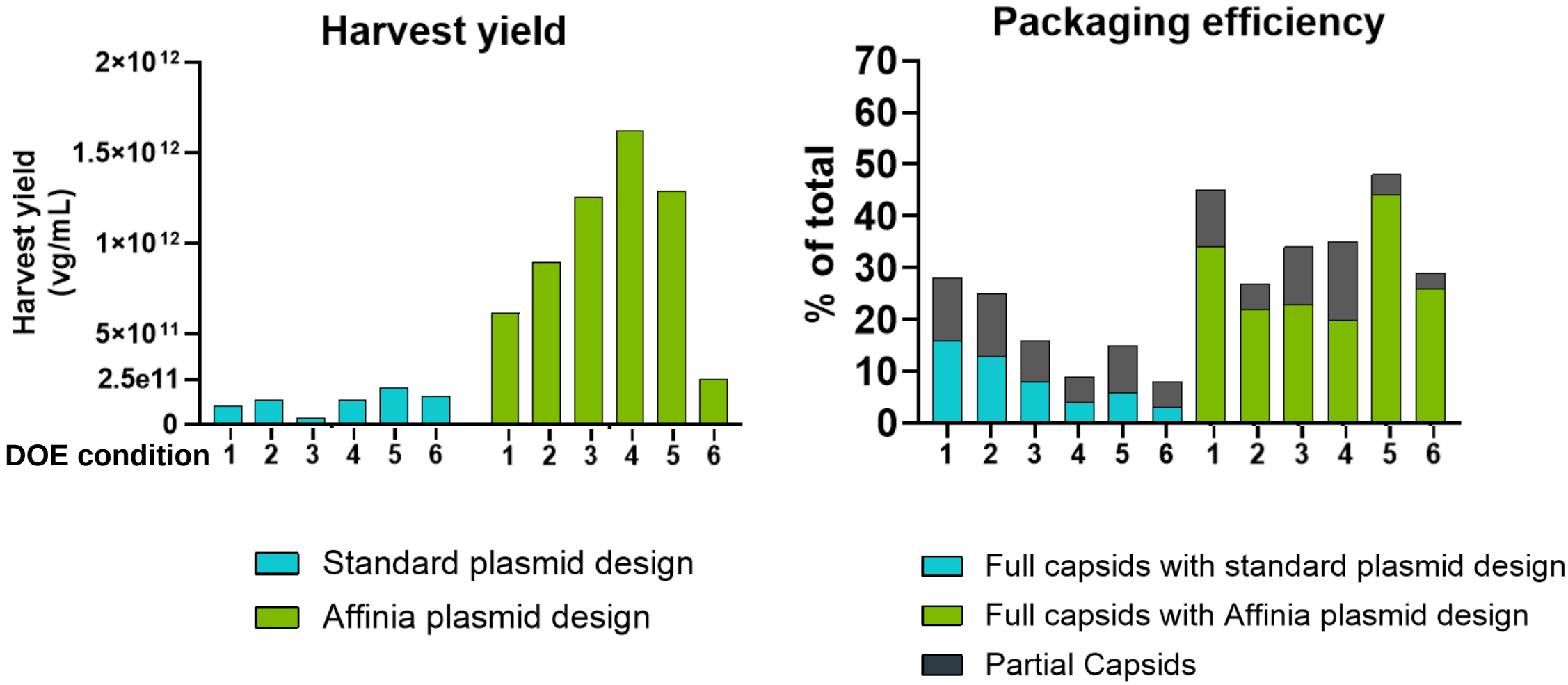




Suspension HEK293
Shake flask
Affinia media

3.8 kb therapeutic transgene
Fectovir

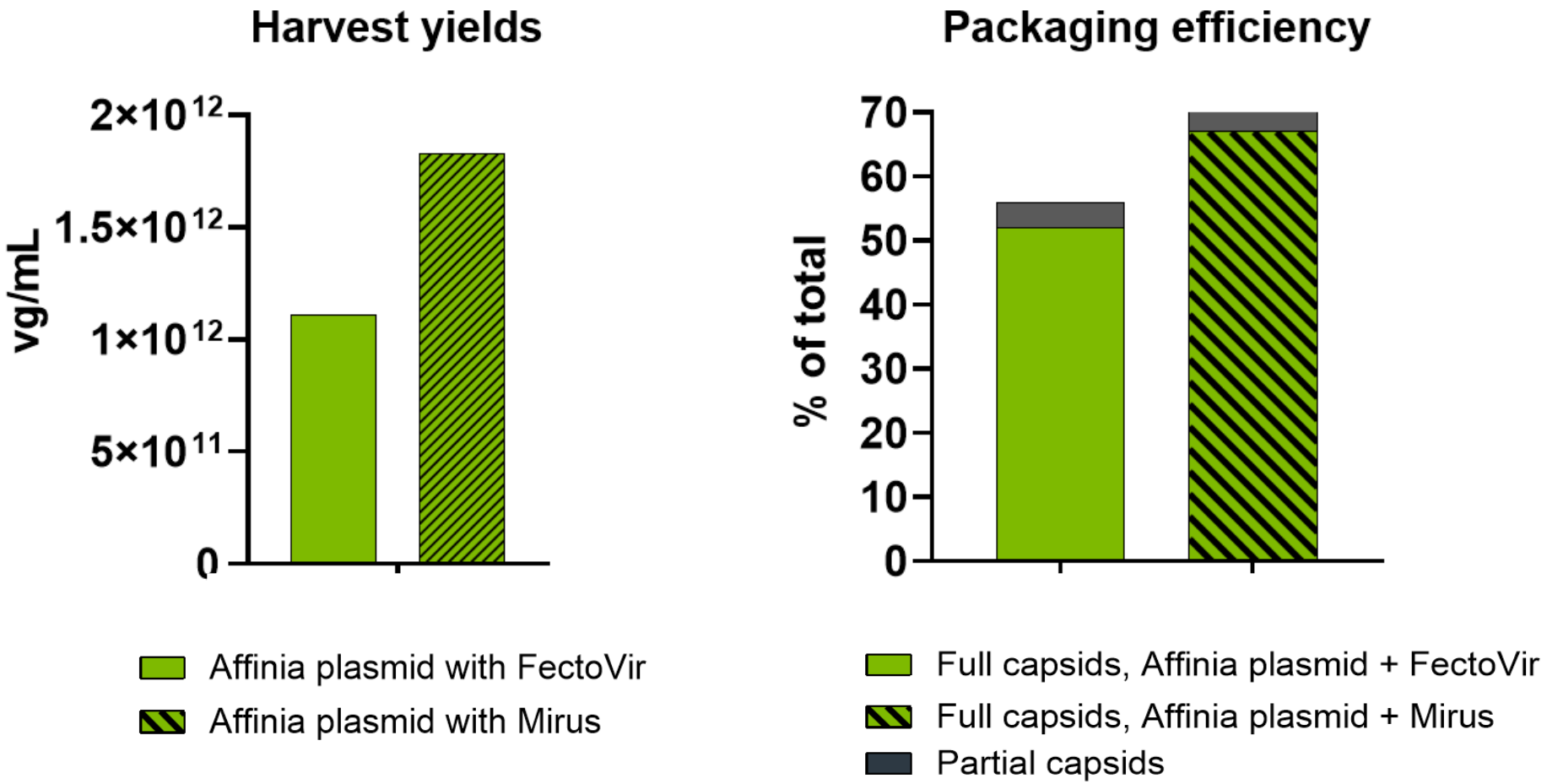
Plasmid design improves productivity of large transgenes



Suspension HEK293
Shake flask DOE
Affinia media

4.7 kb therapeutic transgene
Fectovir
ATC-0109

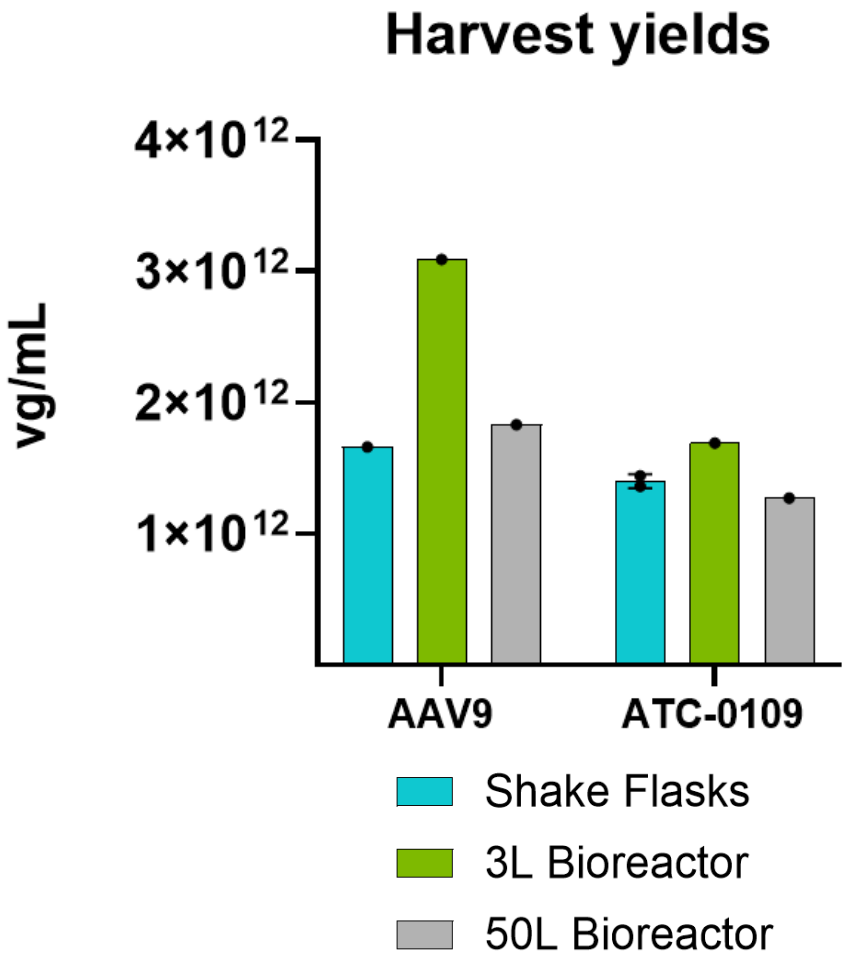
Plasmid design works with multiple transfection reagents

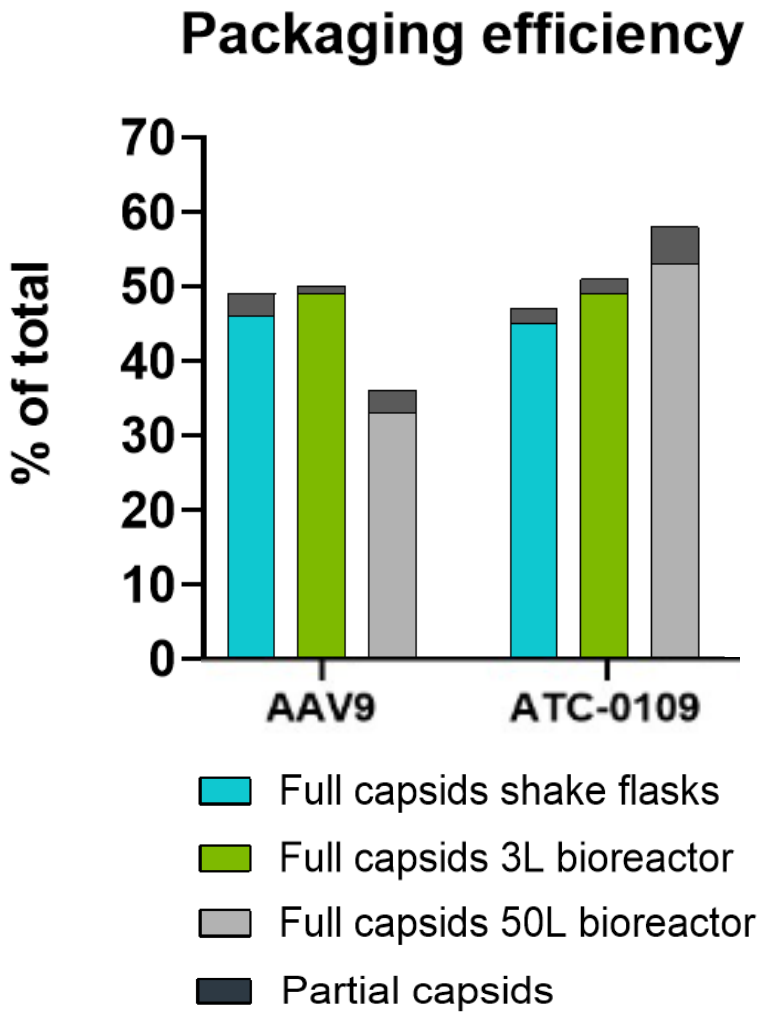


Suspension HEK293
Shake flask
Affinia media

3.2 kb therapeutic transgene
ATC-0109

Affinia plasmid design scales from shake flask to 50L bioreactor





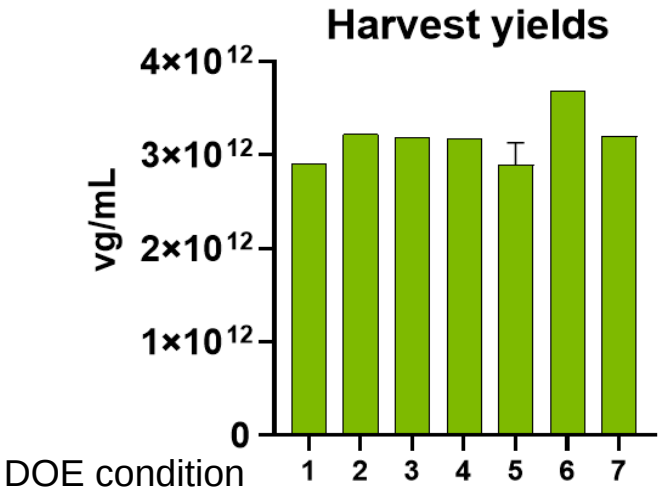
Affinia plasmid design improves other CQAs

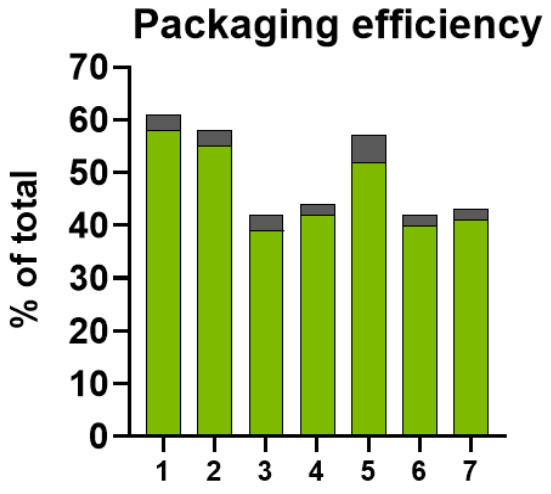
Attribute	Affinia Process	AAV9 example
hcDNA	5-10x reduction	<10pg per 1e9 vg
Residual plasmid DNA	5-10x reduction	E10 per 1e13 vg
Infectivity / In vivo potency	No change	N/A
rcAAV	2-3 log improvement	Negative at 1e11, 1e10 and 1e9

We use this Affinia proprietary plasmid design for all of our preclinical work and intend to use for our clinical programs

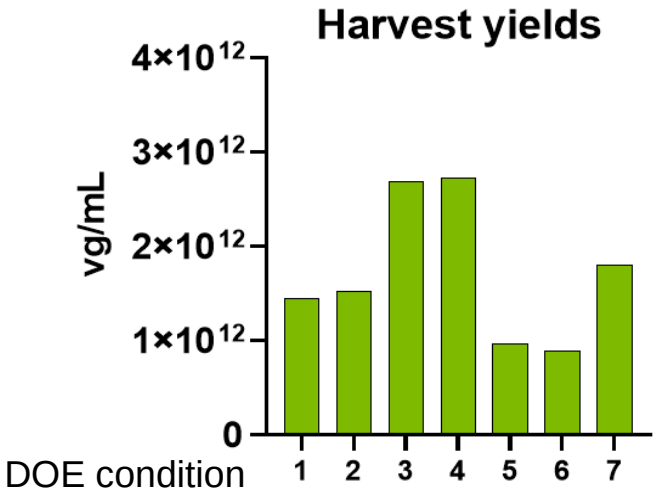
Through use of DOEs we have increased yields to over 3.5e12 vg/mL while maintaining > 40% full capsids

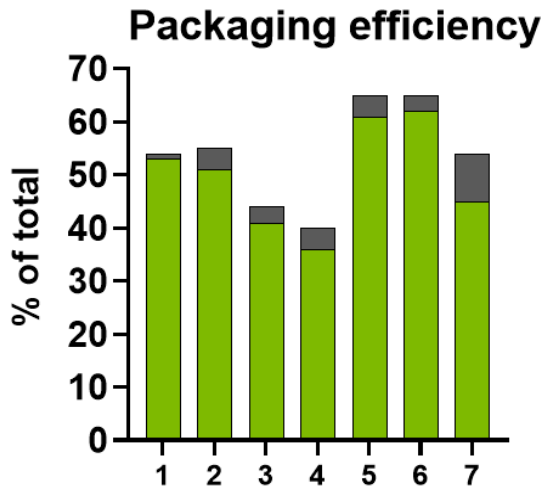
AAV9





ATC-0109





Suspension HEK293
Shake flask
Affinia media

3.2 kb therapeutic transgene
Fectovir

Affinia plasmid design can significantly improve COGs

500L Bioreactor

Standard plasmid design	Affinia plasmid design
1.5e17 total vg at harvest (3e14 vg/L)	1.5e18 total vg at harvest (3e15 vg/L)
>6e16 total vg purified (40% process recovery)	>6e17 total vg purified (40% process recovery)
25 doses (2.4e15 vg total dose*)	250 doses (2.4e15 vg total dose*)

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*Assumes 80kg patient at 3e13 vg/kg

An opportunity to move the field forward

- Our proprietary plasmid design delivers high yields with a high % of full capsids enabling an effective AEX polishing process
- Our proprietary plasmid design is modular and easily implemented into any existing suspension HEK293 process
- We have filed patent applications on this design and related manufacturing process

Contact us

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Acknowledgments

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