GSASA BASEL KONGRESS CONGRÈS 2024

Basel, November 27-29, 2024

Révolutionner les Thérapies Géniques: Réduction des Coûts de Production des Biologiques avec NewBiologix

Revolutionierung der Gentherapien: Senkung der Produktionskosten für Biologika mit NewBiologix

Igor Fisch, PhD

Chief Executive Officer

NEW BIOLOGIX

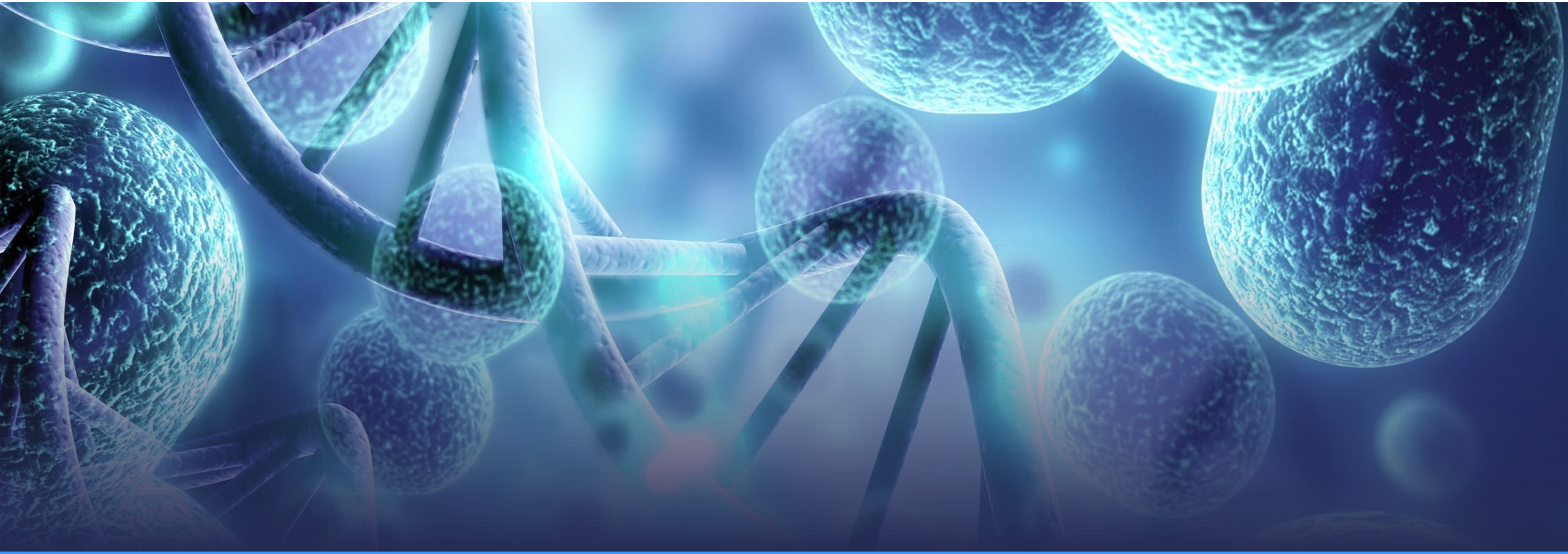
Agenda

1. NewBiologix SA foundation
2. ATMPs: Advanced Therapy Medicinal Products
3. Gene therapy market and challenges
4. NewBiologix’s vision
5. NewBiologix’s products
6. Q&A

Made in Switzerland

Built on an Outstanding Reputation of Exceptional Quality and Innovation

1800m^2 State of The Art Facility Specifically Designed for Advanced Therapies Medicinal Products (ATMPs)



ATMPs

Advanced Therapy Medicinal Products

ATMPs: Advanced Therapy Medicinal Products

What are ATMPs?

Innovative medical treatments using genes, cells, or tissues to **address or cure diseases at their source**

Key Categories of ATMPs	• **Gene Therapy** Medicinal Products (GTMPs): Modify genetic material to treat or cure diseases • **Somatic Cell Therapy** Products: Use cells to repair or replace damaged tissues • **Tissue-Engineered** Products (TEPs): Regenerate tissues using cells and scaffolds • **Combined ATMPs**: Integrate ATMPs with medical devices
Challenges	• High **costs** and **complex** manufacturing • **Ethical** and **safety** concerns with gene editing • **Regulatory** and **logistical** challenges
Benefits	✓ **Personalized medicine** tailored to genetic profiles ✓ Potential to **cure rare and severe diseases** ✓ **Innovation** in regenerative medicine and oncology

Revolution in modern medicine

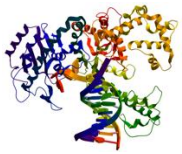
ATMPs: Advanced Therapy Medicinal Products

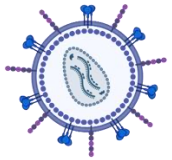
Deliver targeted drugs to cells by physical, chemical, viral or cellular methods


DNA


RNA

Proteins

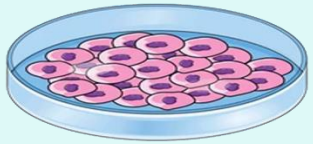



Lentivirus

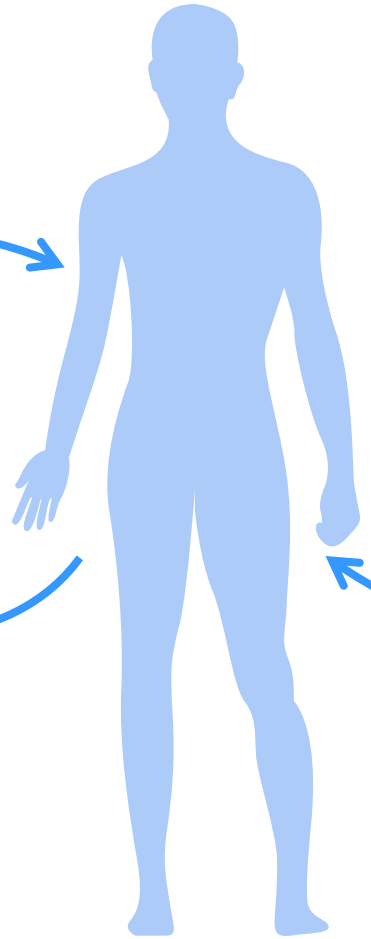

CAR-T cells

Ex vivo

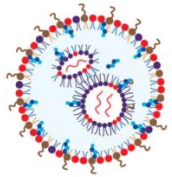
Introduce modified cells back into patients

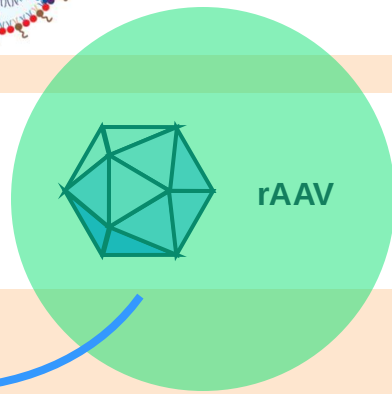


Extract stem or progenitor cells



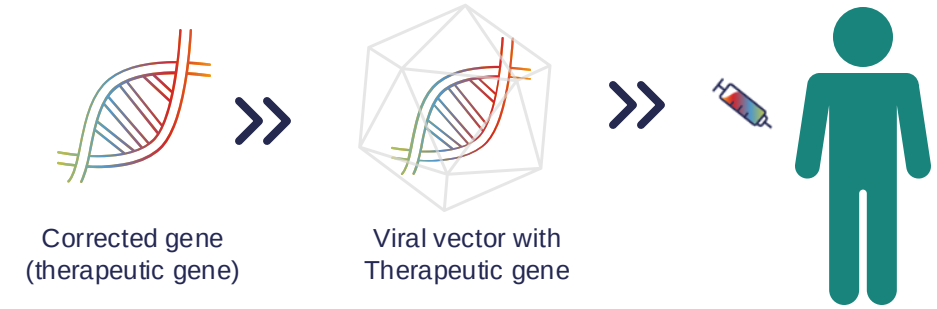
In vivo


Lipid nanoparticles



Direct delivery to patients using viral or non-viral delivery vehicle

Gene Therapies Have the Potential to “Cure” an Array of Rare, Chronic, and Incurable Diseases



1,000 Gene Therapy Programs in the Clinic

12 Approved Gene Therapies Since 2003

LIMITATIONS HAVE HAMPERED PROGRESSION AND ACCESS TO GENE THERAPIES

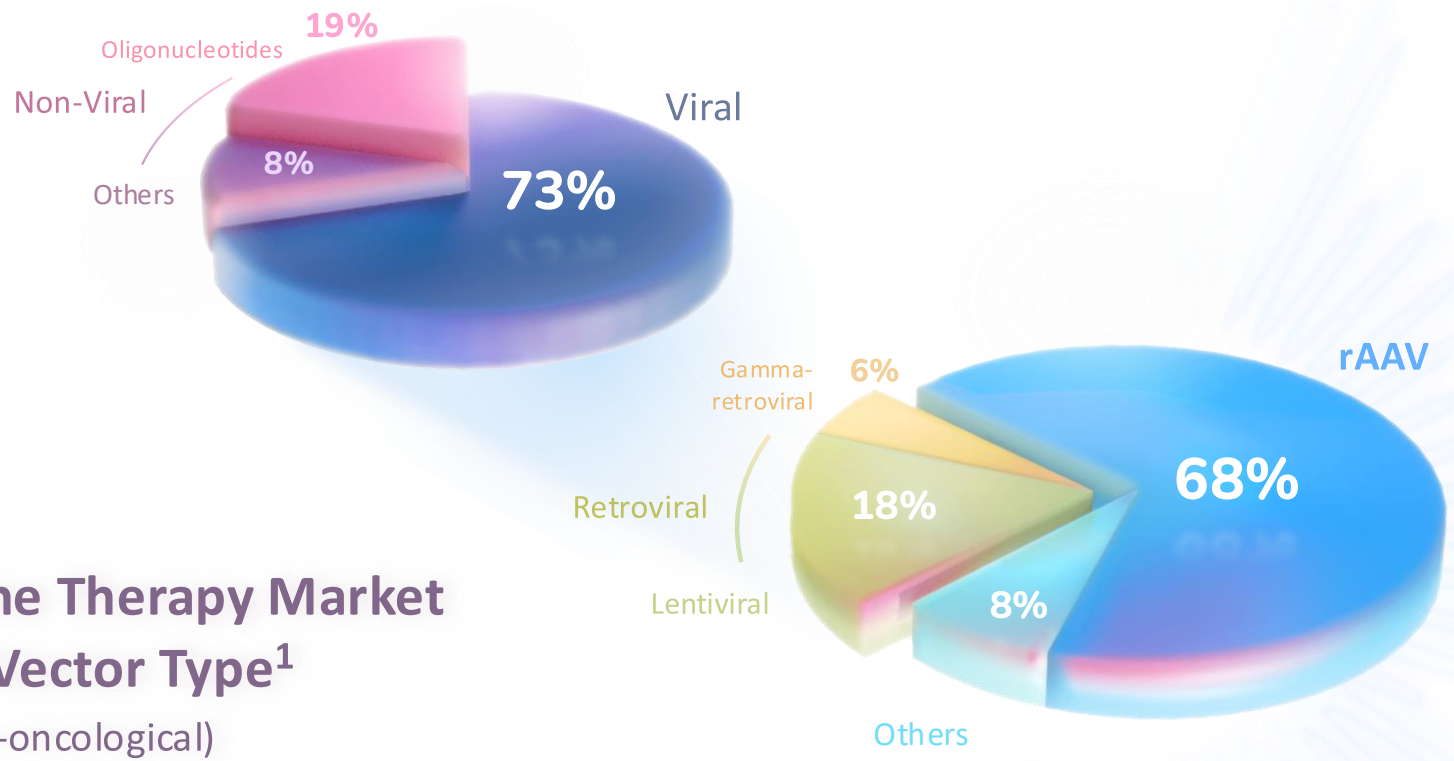
Safety

Efficacy

Costs

CRUCIAL NEED OF SOLUTIONS

rAAV Delivery Is the Primary Vector for Delivering Gene Therapies



Gene Therapy Market by Vector Type[1]

(non-oncological)

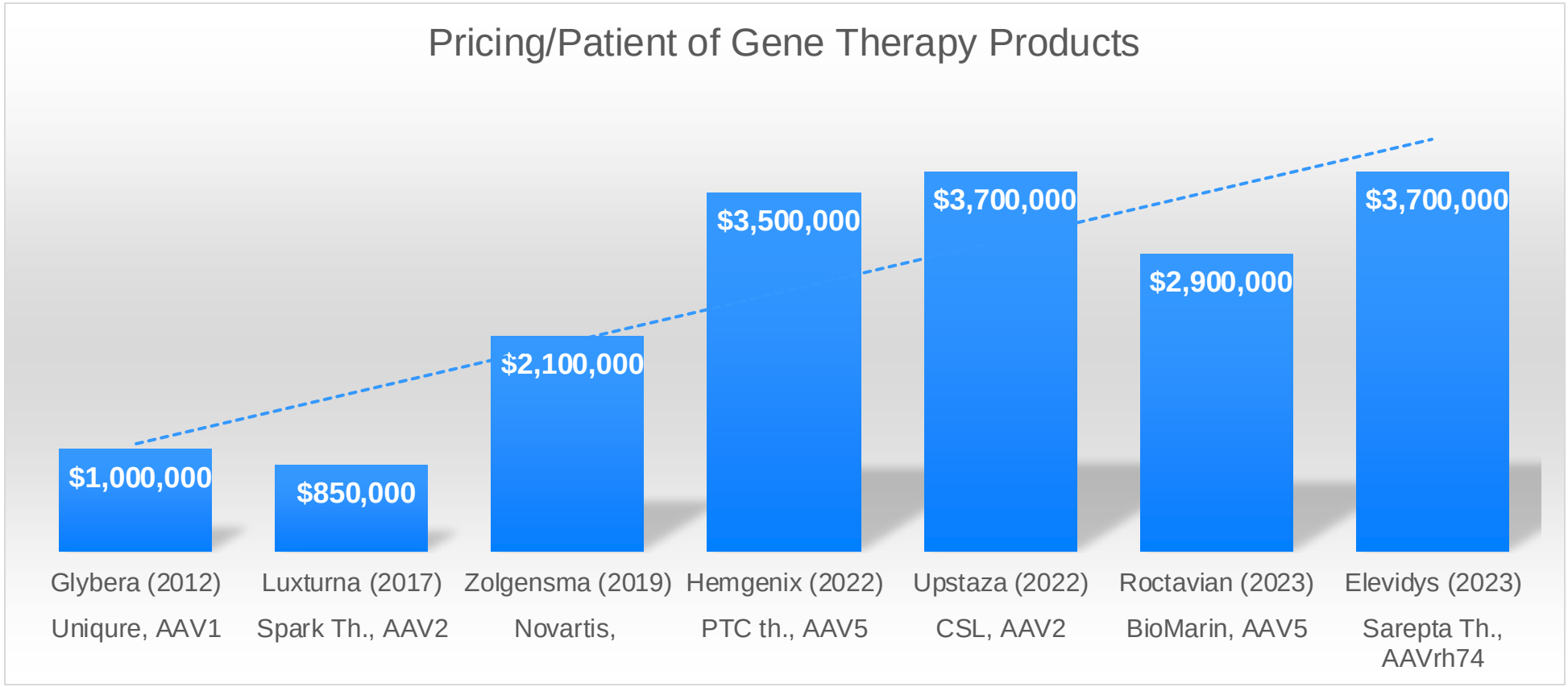
AAV vector platform dominates *in vivo* gene therapy

- ✓ Superior biosafety
- ✓ Broad range of infectivity
- ✓ Low immunogenicity

Sources

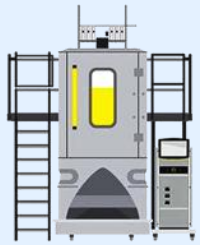
1. Polaris report, 2022, Gene Therapy Market Analysis & Segment Forecast to 2030;
2. Viral-vector therapies at scale: Today's challenges and future opportunities – McKinsey - 2022

Pricing of Current Marketed rAAV Products



1. **Complex**/Expensive Manufacturing Processes
2. **Small** Patient Populations
3. Potentially **Curative** Nature
4. **Regulatory** and Reimbursement Complexity
5. **Ethical** and **Societal** Concerns

Capacity Limitations with Current Production Cell Lines and Technology Platforms

MODALITY	BIOREACTOR	PRODUCTION CAPACITY	DOSE	NUMBER OF PATIENTS TREATED
Antibody	 20,000L	100kg per batch	1 to 50 mg/Kg	**17,500 to 875,000**
Current rAAV Producion	 1,000L	$4x10^{17}$ vg[1] per batch	10^{13} to 10^{14} vg/Kg	**18 to 1,750**

10 to **50,000 X** smaller population

Novel technologies for the production of viral particles for gene therapy

Terrence Dobrowsky et al. Current Opinion in Biomedical Engineering (2021) 20:100353
Aponte-Ubillius, Applied Microbiology and Biotechnology (2018) 102:1045

[1]Viral genome

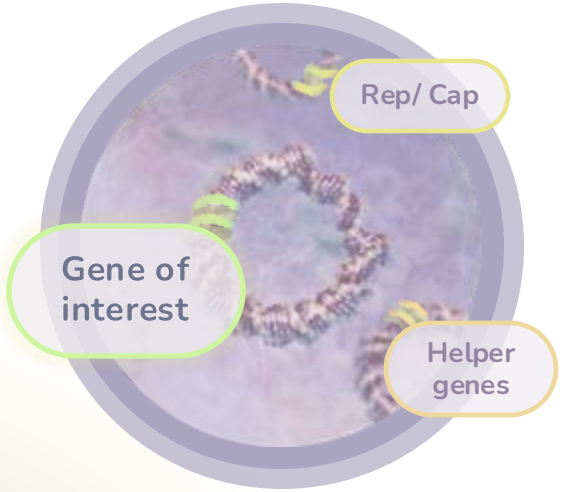
NEW BIOLOGIX

Our Vision

Stable Cell Line for rAAV Production To Address Manufacturing Limitations

The NewBiologix Approach:
A Stable Cell Platform For rAAV Vector Production

Current rAAV



Transient transfection
rAAV/Ad genes

Scalability
Limited

Yield
Variable

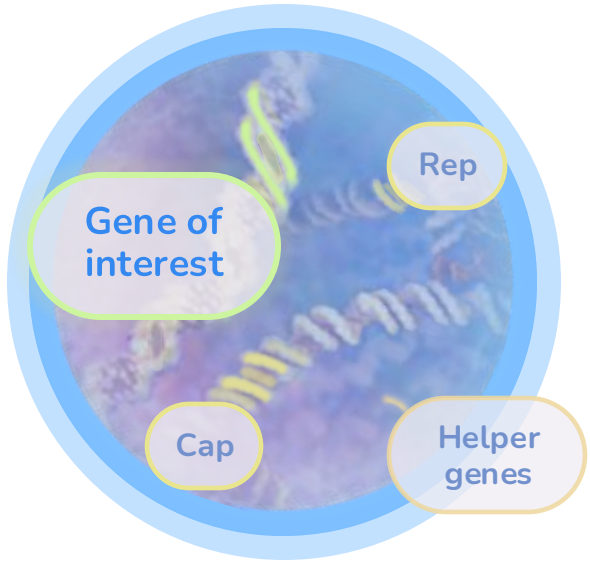
Production Costs
High

Predictability/ Reproducible
Low Reproducibility

Production System
Non-Inducible

Full/ Empty Capsid Ratio
Variable

NewBiologix



Stable transfection
rAAV/Ad genes

Scalability
✓ Highly scalable

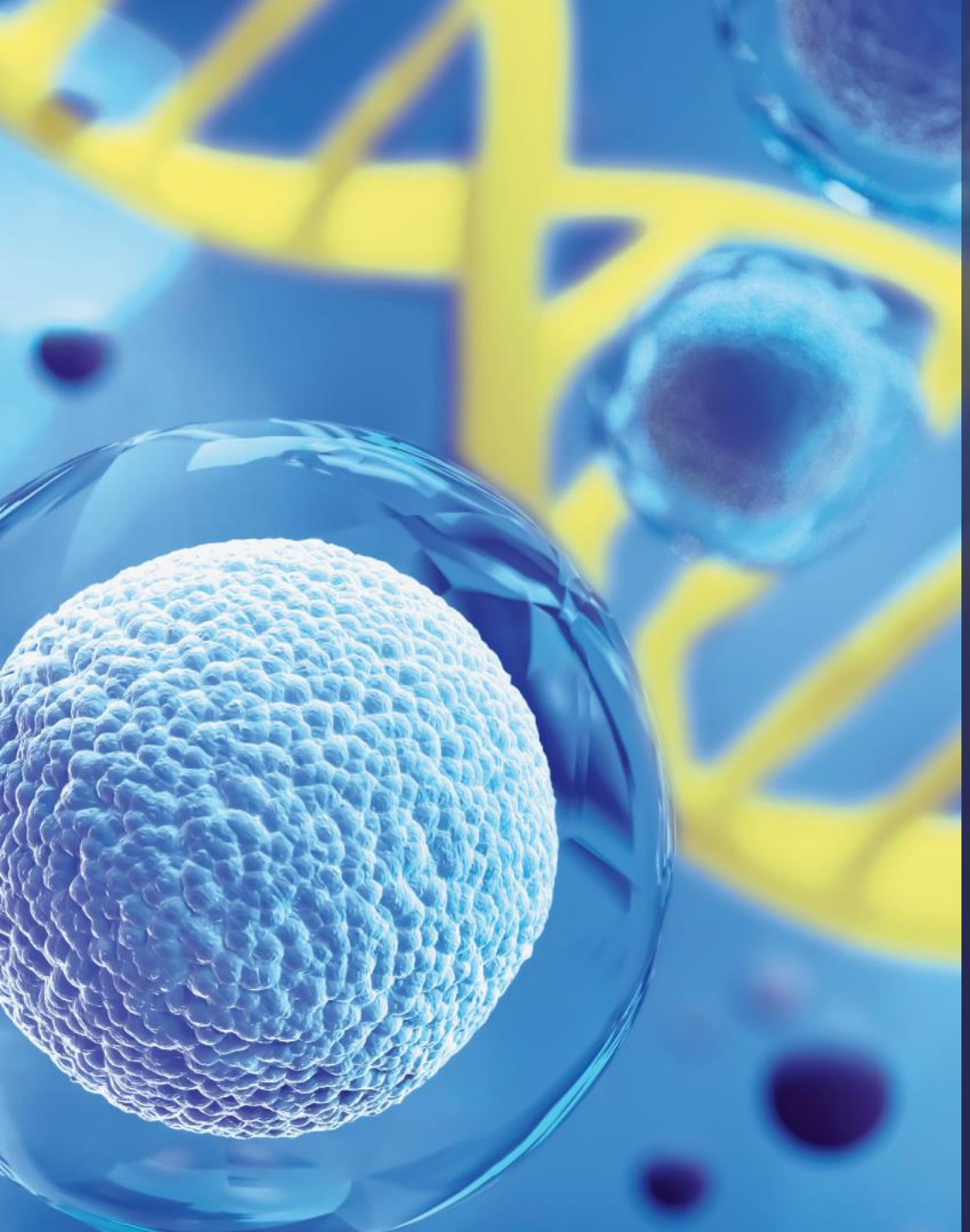
Yield
✓ Consistent

Production Costs
✓ Reduced

Predictability/ Reproducible
✓ High Reproducibility

Production System
✓ Inducible

Full/ Empty Capsid Ratio
✓ Optimized

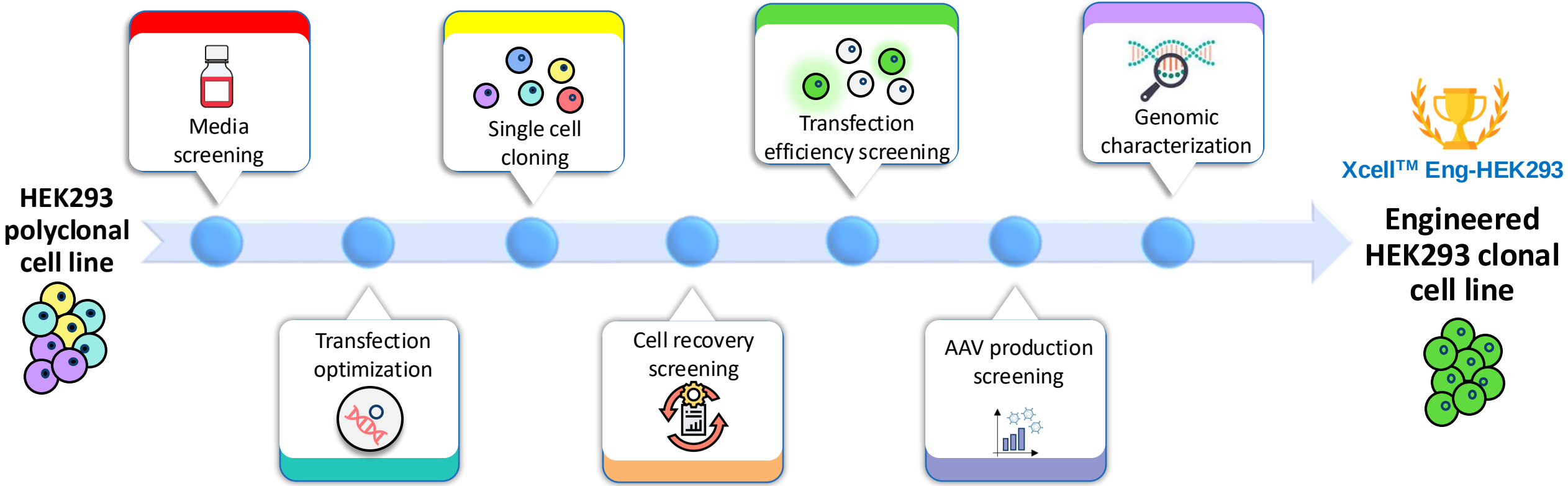


Proprietary NewBiologix Engineered HEK293 Cell Line

Xcell™ Eng-HEK293

NEW BIOLOGIX

Xcell™ Eng-HEK293: Development Process Overview



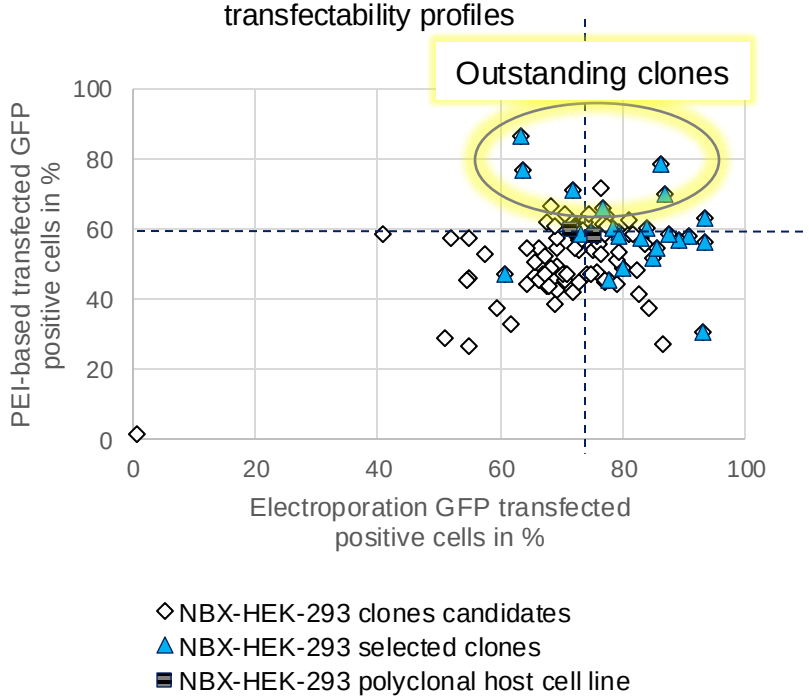
Xcell™ Eng-HEK293: Transfection and Production Features

Suited for high-efficiency transient & stable transfection

Engineered cell clones selected for higher rAAV production

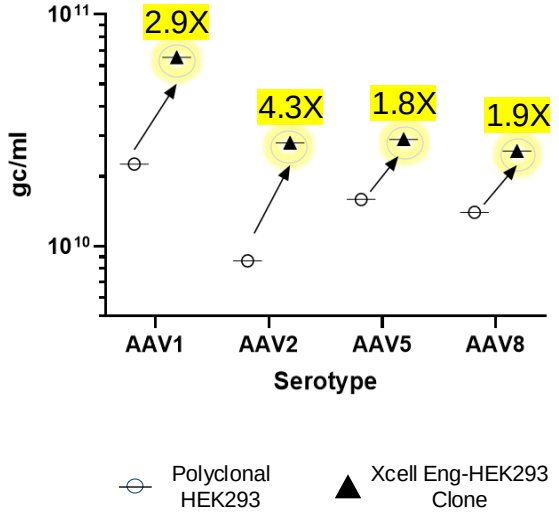
High Transfectability

Identification of Xcell™ Eng-HEK293 Clones with superior transient and stable transfectability profiles



Superior rAAV Titers

Superior rAAV titers using Xcell™ Eng-HEK293 Clones compared to the Polyclonal HEK293



Xcell™ Eng-HEK293: Productivity Features During Process Development

Comparable AAV titers with leading commercial cell lines, making Xcell™ Eng-HEK293 a reliable choice for viral production.

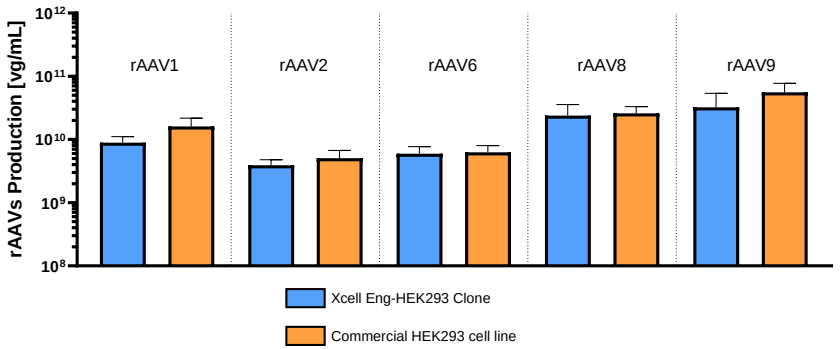
Consistent titers of AAV production across different volumes, ensuring scalability without compromising yield.

Capability to produce AAV for various therapeutic genes and gene sizes, demonstrating its potential for clinical applications.

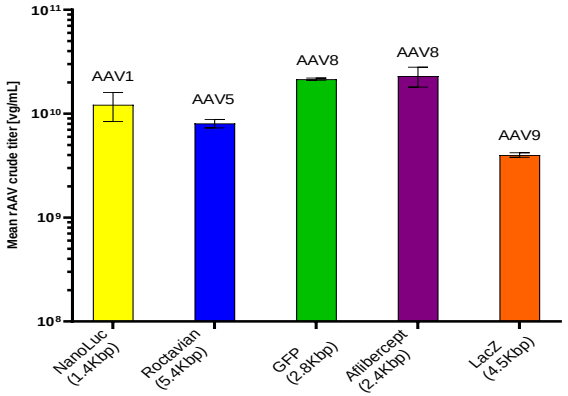
Consistent AAV productivity over passaging, underscoring their reliability for process development.

rAAV Titers

Comparable rAAV titers with leading commercial cell line

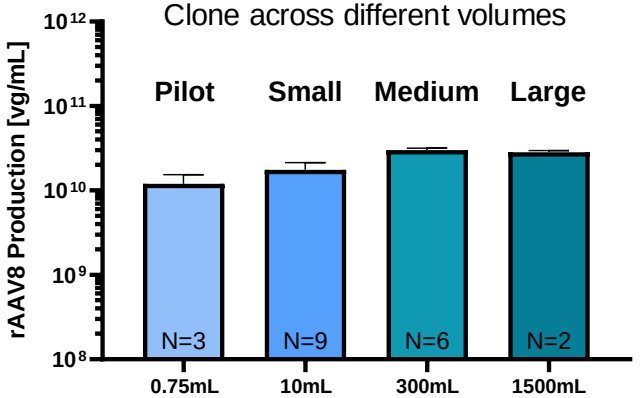


Different Gene Of Interest



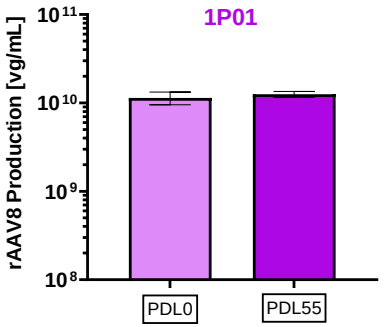
Scalability

rAAV production in Xcell™ Eng-HEK293 Clone across different volumes



Stability

rAAV production in Xcell™ Eng-HEK293 after 55 generations



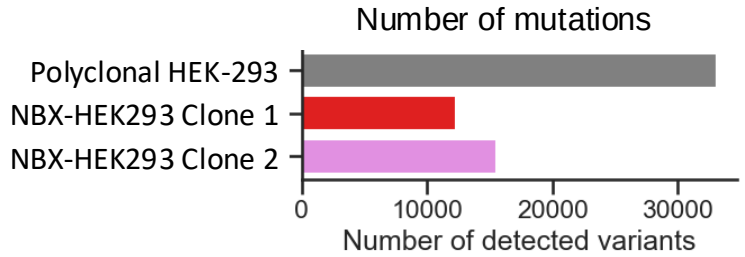
Xcell™ Eng-HEK293: Genomic Characterization by NGS

Fewer genomic variants in NBX' cell clones

Fewer genomic rearrangement in NBX' cell clones

Chromosomal stability for long-term and bioreactor cell culture applications

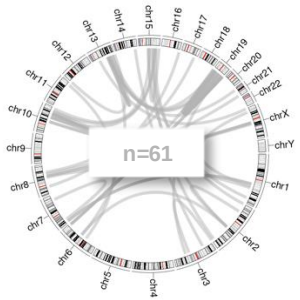
Genomic Mutations



Mutation burden in engineered HEK-293 cell clones
Number of unique SNPs detected in each clone compared to the polyclonal population

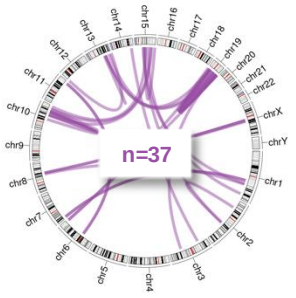
Structural Rearrangements

Polyclonal HEK293



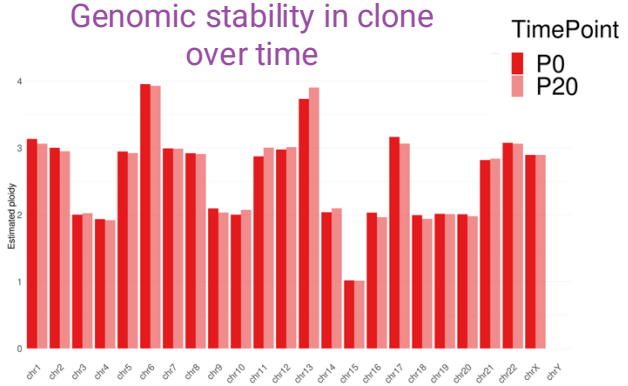
61 translocations

Xcell™ Eng-HEK293



37 translocations

Genomic Stability



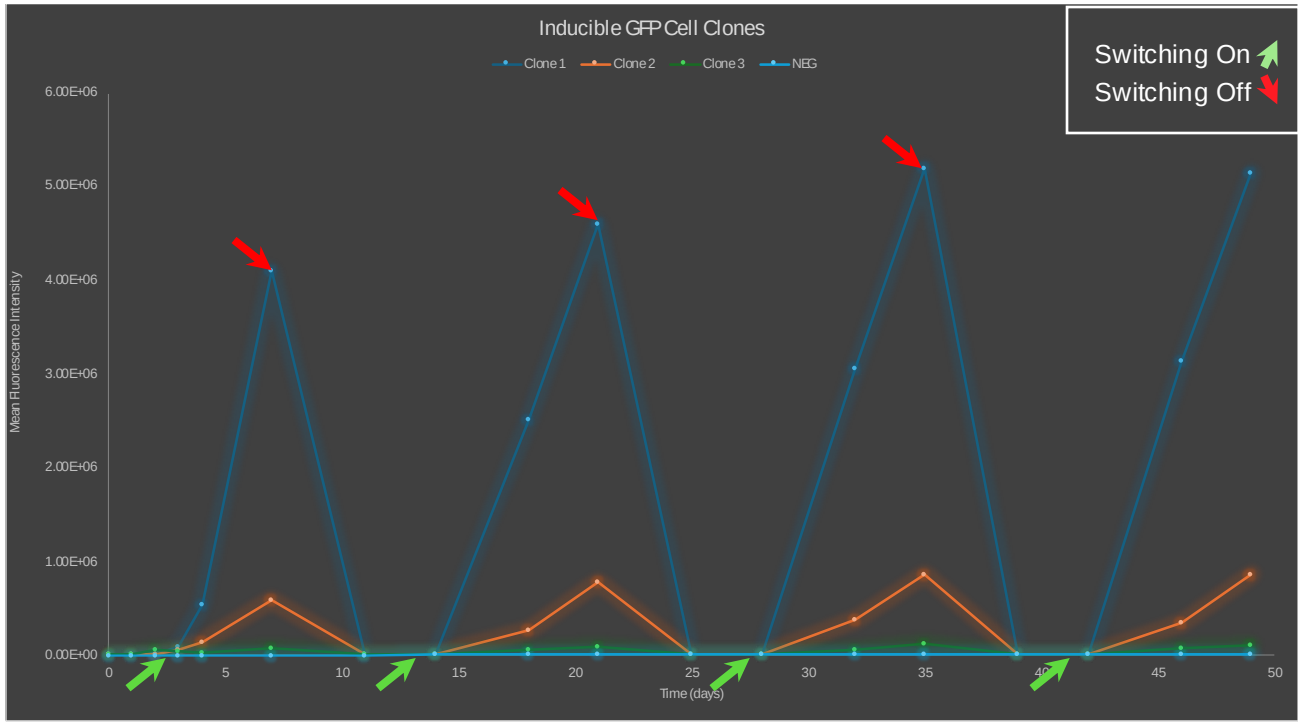
NEW BIOLOGIX

Towards a Stable Production Platform

Construction of Regulatory Network System

A Functional Regulatory Network System (RNS) in HEK-293

Construction and **validation** of cell clones that contains a RNS system and respond to On/Off switching



Functional Regulatory Network System (RNS) validated

NewBiologix’s Product Offerings

NEW BIOLOGIX

Product 1

Xcell™ rAAV Production Platform for Preclinical testing

Opportunities For Testing Various rAAV Candidates

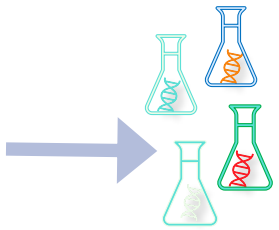
DNA construction | **Transfection** | **Purification** | **Analysis** | **Shipment**

rAAV candidate 1
GGGAACCGTTACGGCG

rAAV candidate 2
CTTTAGCCTGGCCGTC

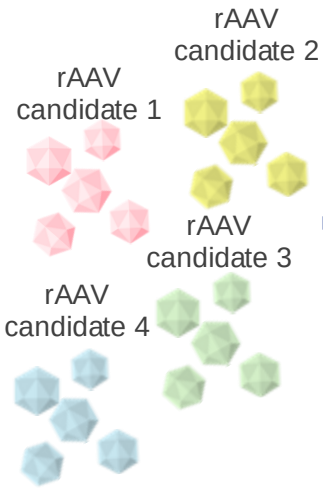
rAAV candidate 3
CATCCATGGCTGAAAC

rAAV candidate 4
CTGTTGCCAGTGCCTA



Testing of different GOI and CAP

Small-scale production
@different scales



- ✓ rAAV sample
- ✓ Capsid Titer
- ✓ Full/Empty capsids
- ✓ rAAV genome QC

Xcell™ rAAV Production Platform

Xcell™ rAAV Purification Platform







Production & harvesting → HFF concentration → Affinity purification → AEX → Sterile filtration → UF/DF

Purified rAAV

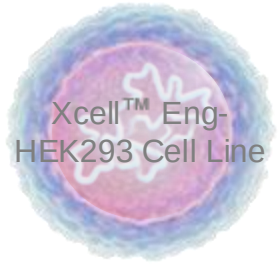
NewBiologix purification platform is closely aligned with large-scale and clinical production standards

NEW BIOLOGIX

Product 2

Xcell™ rAAV Analytical Platform

Xcell™ rAAV Analytical Platform Overview



rAAV Production

Affinity+Anion exchange Chromatography

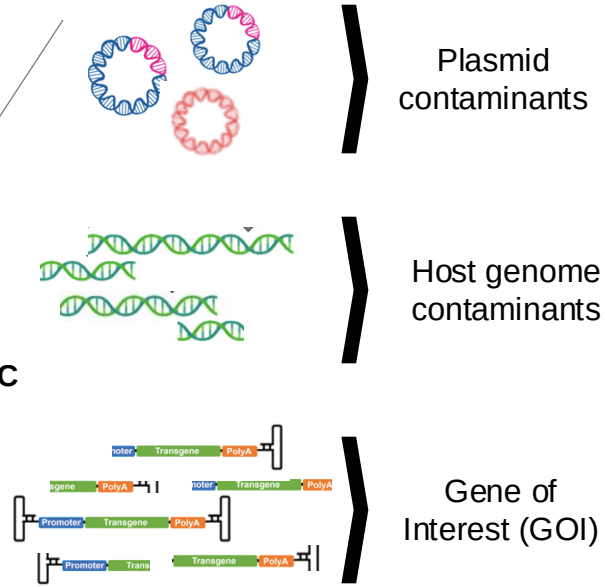
Full capsid enrichment

Purified rAAV

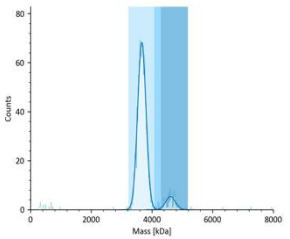
DNA extraction

rAAV QC

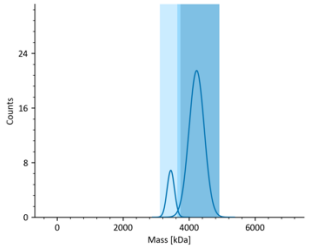
rAAV titration



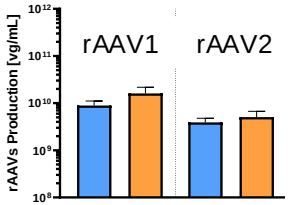
Mass Photometry
Full/Empty capsid



Mass Photometry
Full/Empty capsid

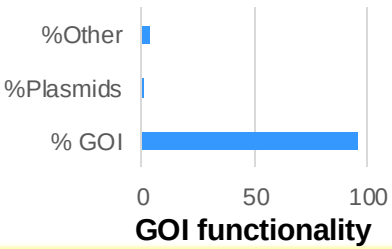


dPCR
Titration vg/mL

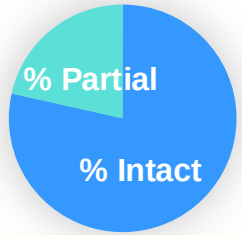


Quality Control:
- Transient production
- Stable production

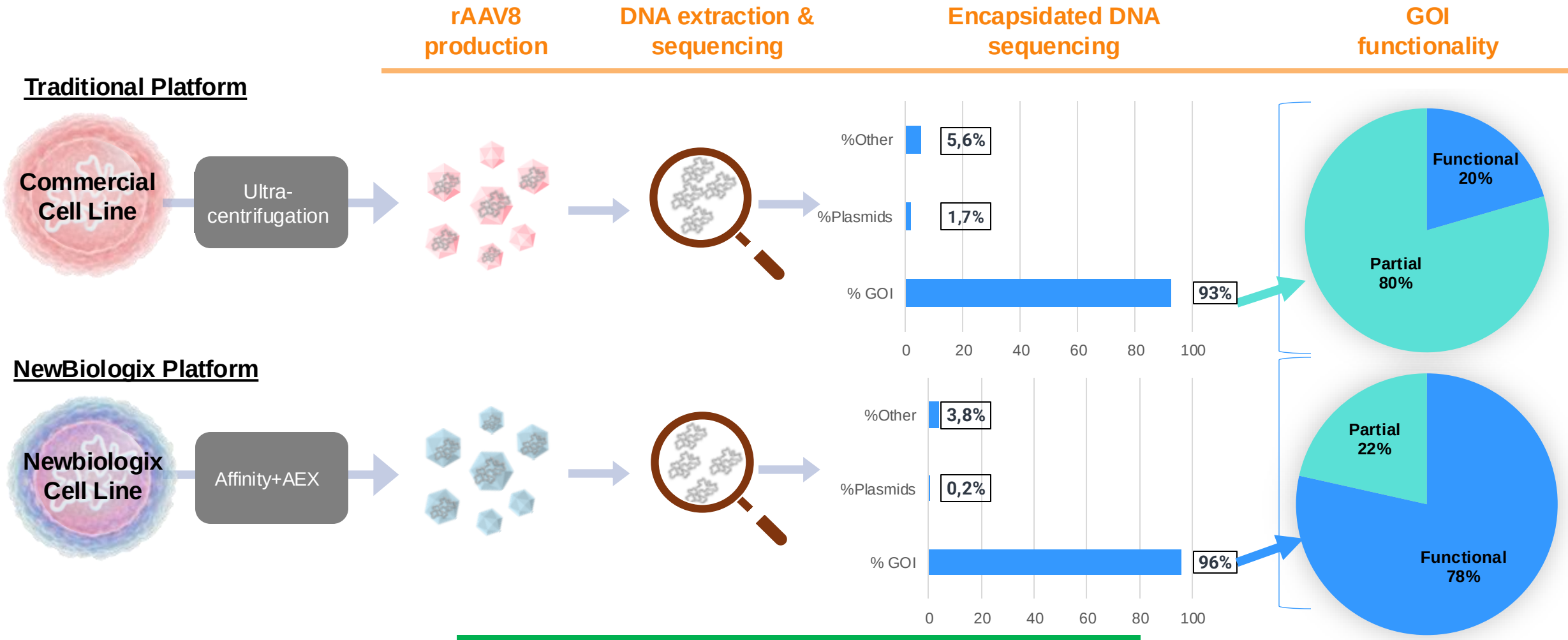
NGS
PacBio/Nanopore



PacBio and/or dPCR
GOI functionality



Xcell™ rAAV Encapsidated DNA Functionality



NBX analytical platform allows **precise characterization** of rAAV preparations

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Conclusions

Mar. 2022: Launch a start-up to address gene therapy manufacturing

Apr. 2022: Build a worldclass team to achieve the objectives and SAB

Sep. 2022: Start building R&D laboratories dedicated to advance ATMPs

May 2023: Cut the ribbon of NewBiologix SA laboratories

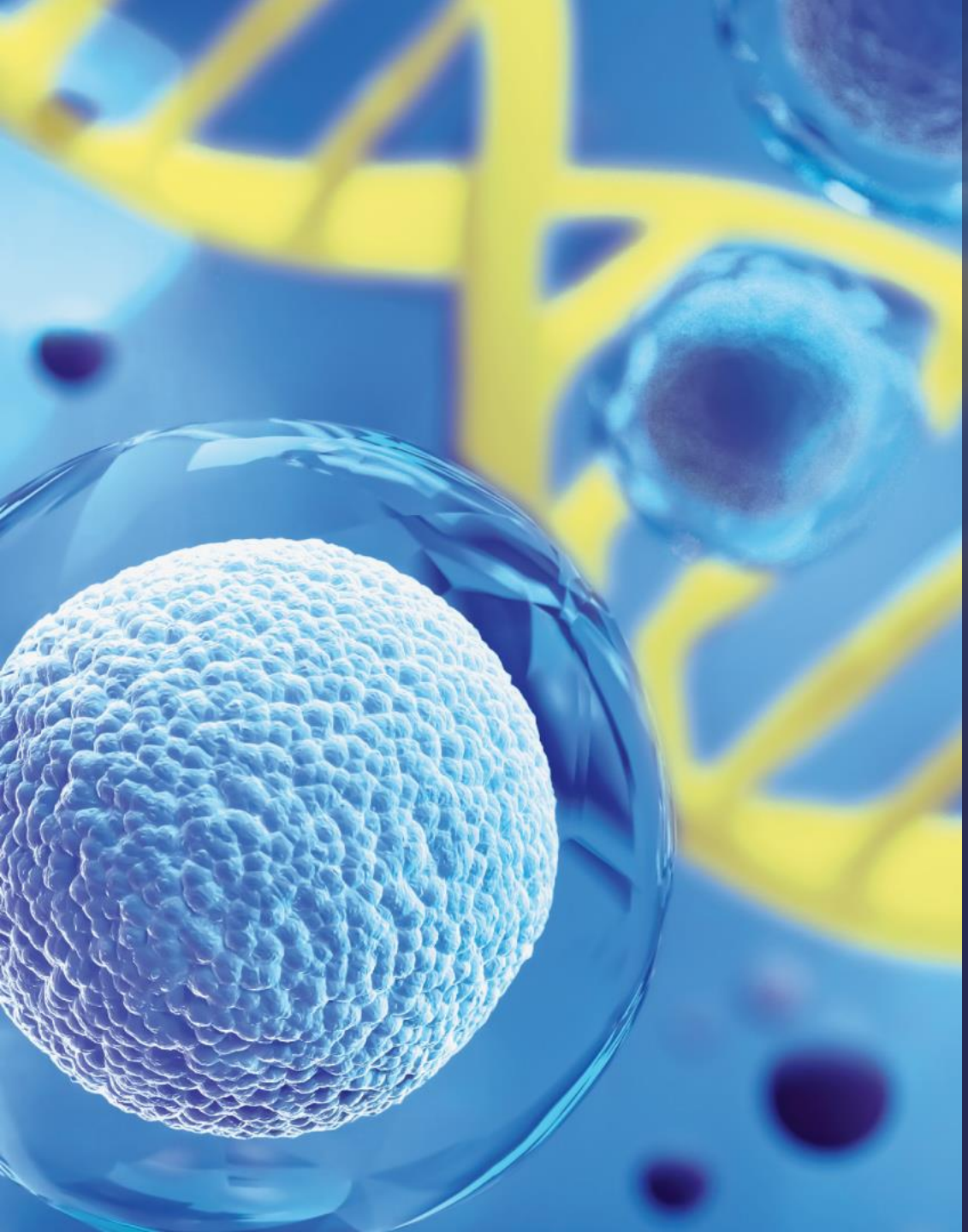
Jan. 2024: Generation of a NBX engineered HEK-293 clonal cell line

Jun. 2024: Validation of a Regulatory Network System (RNS) in HEK-293

Sep. 2024: Product 1 - Transient production platform for preclinical testing

Oct. 2024: Product 2 - Full NGS analytical platform

Dec. 2024: NBX first patent applications



THANK YOU!

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