A Next Generation Platform for Genetic Medicine Manufacturing

appliedDNAsciences

Nasdaq: APDN

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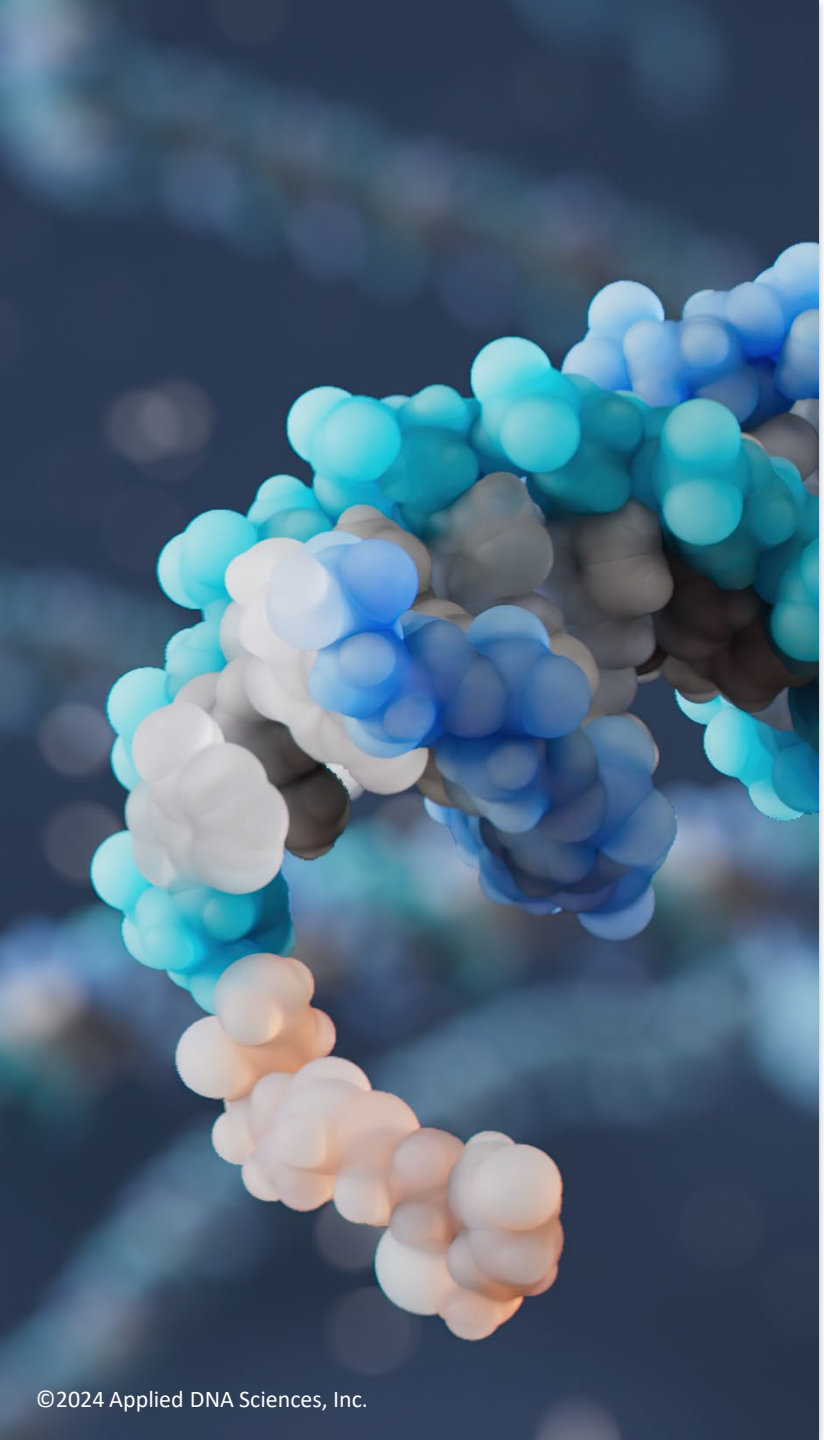


Company Overview

- 3 interrelated business segments all leveraging the polymerase chain reaction (PCR) to enable manufacture and analysis of DNA
  - **Therapeutic DNA Production**
  - MDx and Genetic Testing
  - DNA Tagging and Authentication
- 15 years of experience in enzymatic DNA production
- Growth in genetic medicine development pipelines accelerated pivot to therapeutic DNA production
- 55 employees located in 30,000 sq. ft. facility in Stony Brook, New York

Investment Highlights

- Pioneering enzymatic therapeutic DNA production for next generation genetic medicines as a direct replacement for plasmid DNA (pDNA)
- Patented and patent-pending expertise in the production of DNA via PCR at very large scale
- The largest enzymatic DNA manufacturing company in North America
- Initial opportunity: critical starting material for mRNA therapeutics
- Proprietary platform combining two mRNA critical starting materials outclasses conventional production methods
- Marquee RUO-scale customer base: from Big Pharma to CDMOs
- Imminent, Potential Near-Term Catalysts (CY2024)

Multiple Potential Near-Term Catalysts (CY24)

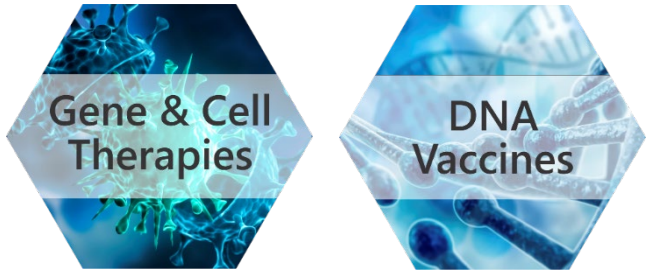
	Q1'CY24	Q2'CY24	Q3'CY24	Q4'CY24
Initiate pursuit of FDA Advanced Manufacturing Technology Designation[1]				
Launch GMP manufacturing capacity for mRNA critical starting materials[2]				
Anticipate signing supply agreements for Linea™ DNA IVT templates/Linea IVT platform				
Anticipate PGx test approval[3]; launch of testing service				
Anticipate initiation of new cotton supply chain				

[1] Proposed designation announced by FDA in December 2023. Pursuit contingent upon final approval of program by FDA
[2] Subject to future ability to raise necessary capital
[3] Approval contingent on length of New York State Department of Health review that is outside of the control of the Company

Genetic Medicine Starts with DNA

Broad Relevance to a Rapidly Growing Opportunity

Linea™ DNA



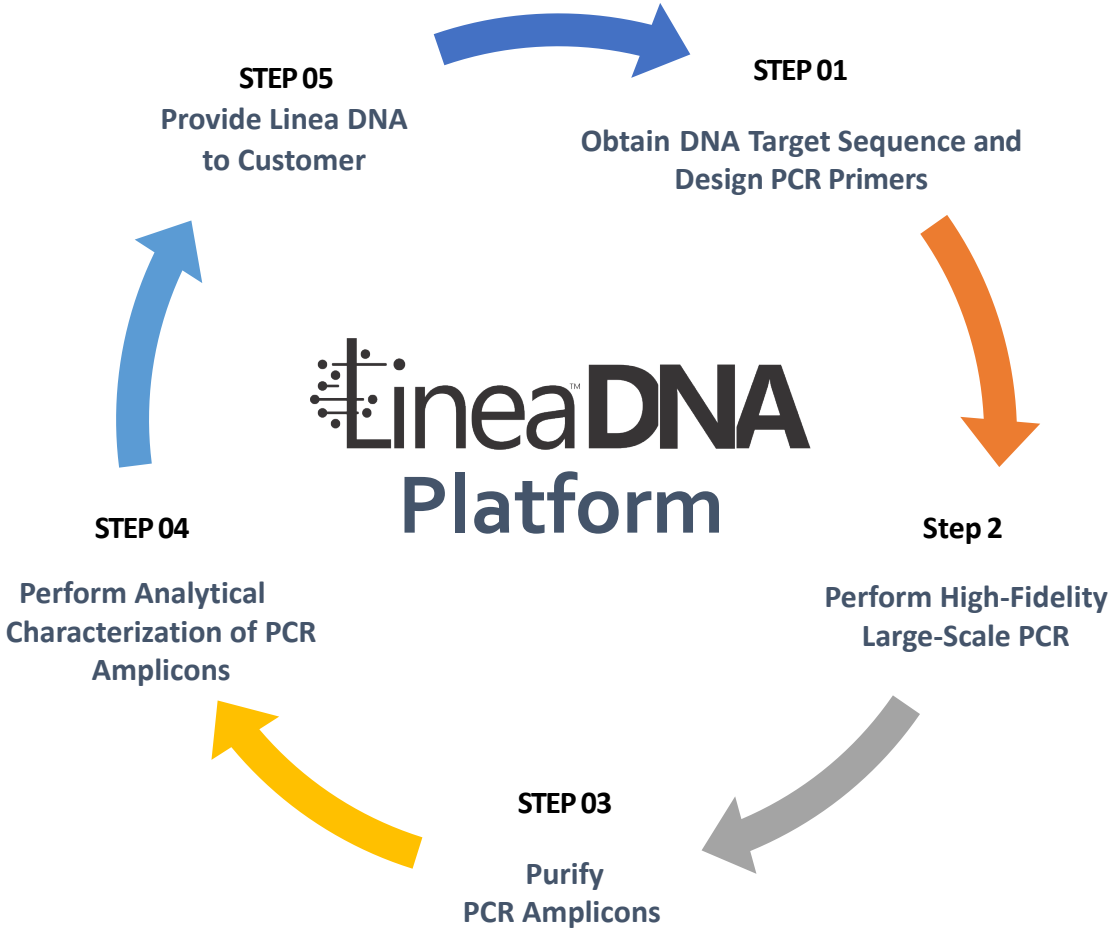
Linea™ IVT

- Over 3,800 genetic medicines in development, almost all in early stages
- 350 mRNA therapies in development - over 68% still in pre-clinical development
- Disease indications range from oncology, gene therapy, rare disease, autoimmune and vaccines
- mRNA manufacturing market forecasted to reach $22.6B in 2031
- First sa-mRNA vaccine approved. mRNA RSV vaccine approval pending

Source: Q3 2023 Gene, Cell & RNA Therapy Landscape, American Society of Gene and Cell Therapy, April 2023
Source: https://www.globenewswire.com/en/news-release/2023/02/21/2612419/0/en/mRNA-Manufacturing-and-Synthesis-Services-Market-worth-22-6-Billion-by-2031-Driven-by-Increasing-Number-of-Clinical-Trials-InsightAce-Analytic.html

LineaDNA Platform

DNA Made Simple



- Only 4 input ingredients
- 5 production steps
- Can be completed in under 2 weeks
- Uses enzymes and is 100% cell free
- Large yield in small footprint
- Uses scalable benchtop instruments
- Simple process is well suited to cGMP

LineaDNA

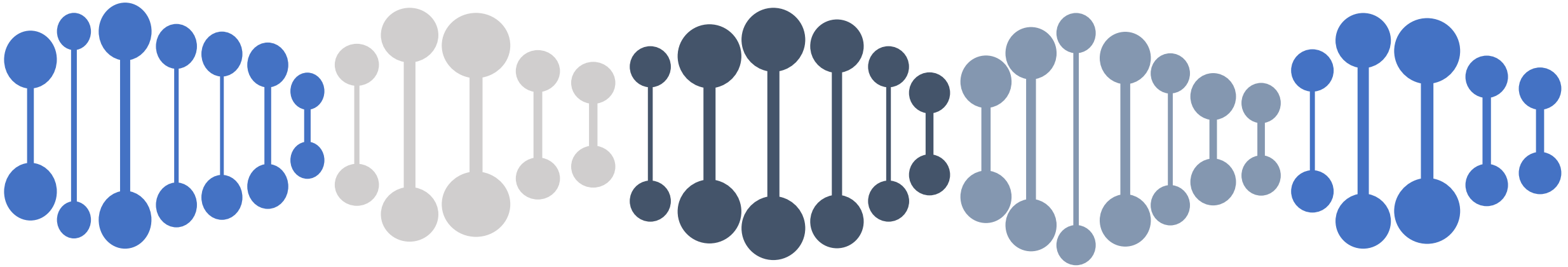
Advantages over plasmid DNA (pDNA)

Purity

Produce Only the
DNA You Want

Flexibility

Chemical Modifications
Various templates



Simplicity

Simplify
Genetic Medicine
Manufacturing

Speed

Milligrams in 14 days
Grams in ≈ 30 days

Scalability

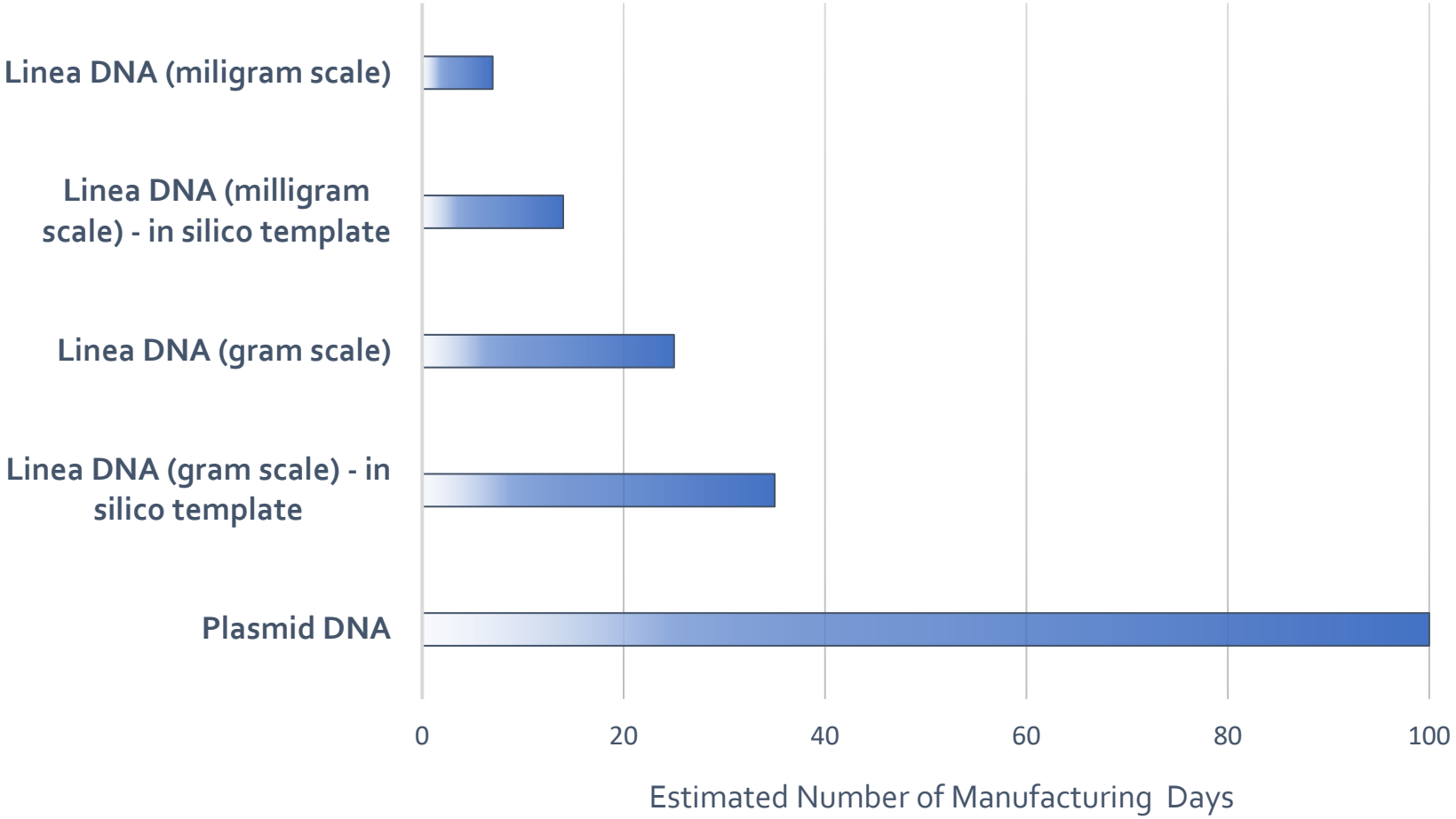
Milligrams to Multi-Grams

LineaDNA Fact Sheet

Attribute	Specification
Physical Structure	Double Stranded DNA (dsDNA)
Size	100bp to 18,000bp
Manufacturing Method	PCR - 100% Enzymatic
Homopolymer Capacity	Up to 150nt with high homogeneity
% Target DNA Sequence	100%
Ready to use for IVT	Yes
Sequence Fidelity	• Observed amplification system fidelity of 66x of WT Taq[1] • Deep NGS sequencing (over 30k read depth) detected no variants as compared to parental pDNA template[2] • Resultant RNA fidelity meets or exceeds pDNA-based RNA[3]
Manufacturing Speed	• Milligrams in ≈2 weeks • Grams ≈ 30 days
GMP Status	Expected online in 1HCY2024[4]

[1] Observed via fidelity assay analysis of 3kb DNA construct
[2] Based on analysis of 2.3kb and 9.5kb DNA constructs
[3] Error rate analysis performed via deep read NGS
[4] Subject to future ability to raise capital

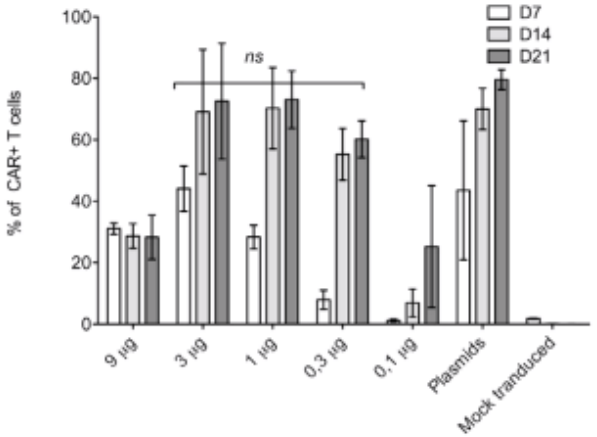
Unparalleled Production Speed



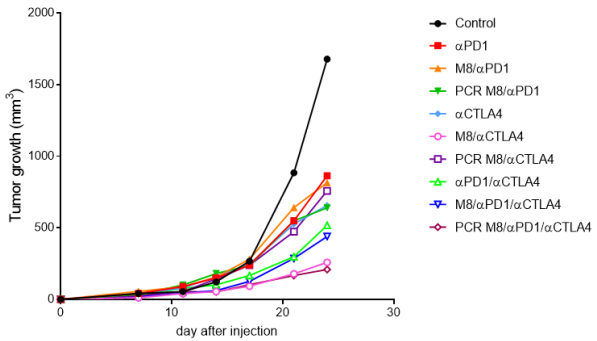
- Ultra-rapid DNA manufacturing
- Little optimization needed for new DNA constructs
- Optimal for R&D, drug discovery, clinical and commercial production workflows
- Capable of using a broad range of template material

Success Across Genetic Medicine Modalities

Oncology

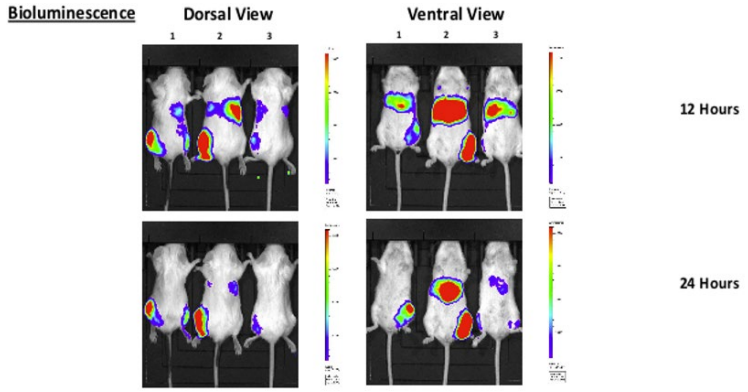


CAR-T Manufacture

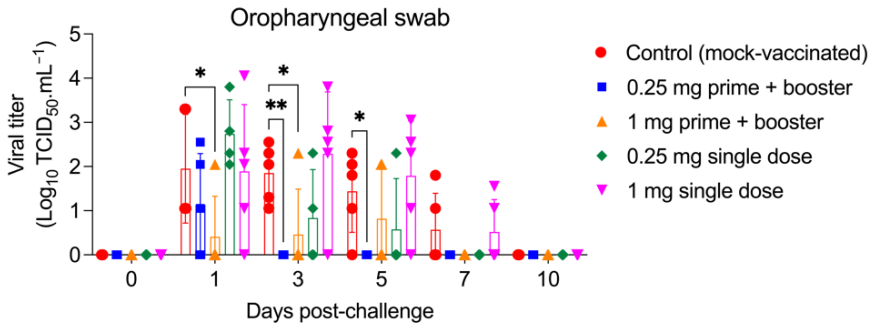


Neoantigen DNA Vaccine

DNA Vaccines

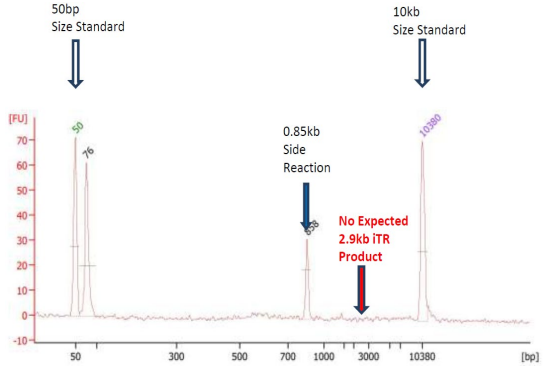


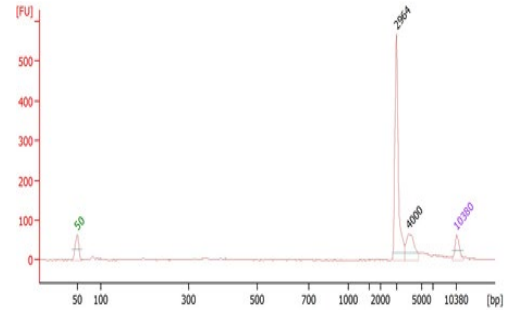
LNP/DNA IM Administration



Protective Prophylactic DNA Vaccine

Gene Therapy





AAV ITR-Transgene Production

Selected Customer Profiles

Broad Relevance Results in a Diverse Customer Base

Gene Editing

- Application - CRISPR-mediated homology directed repair (HDR)
- Requirement - Linear dsDNA comprised of 100% target sequence at large scale
- Outcome - Higher "knock-in" efficiencies than pDNA resulting in successful customer project and repeat orders

Vaccines

- Application - Self-amplifying mRNA (sa-mRNA)
- Requirement - Linear dsDNA IVT template over 10kb in length with large homopolymer sequence
- Outcome - Successful production of sa-mRNA template that customer could not reliability produce in pDNA. Repeat order obtained.

Adoptive Cell Therapy

- Application - CAR-T Therapy
- Requirement - Non-viral DNA expression vector to produce anti-CD19 CAR-T
- Outcome - Successful production of CAR-T cells with high efficiencies and therapeutic index without the use of viral vectors or pDNA. Customer therapy slated for clinic in late CY2024

In vitro Diagnostics

- Application - Hepatic Cancer diagnostic
- Requirement - Very large-scale dsDNA with chemical modifications
- Outcome - Successful production of multiple grams of chemically modified dsDNA leading to long term supply contract

Conventional mRNA Manufacturing Problems

Bacterially derived pDNA is currently the starting material for mRNA

Long lead times increase mRNA production timeline

Struggles with complex DNA sequences such as Poly(A) tails

Requires expensive enzymatic linearization and additional filtration steps

Increased regulatory scrutiny

Plasmid DNA

Double Stranded RNA

Problematic inflammatory byproduct of conventional IVT

dsRNA removal is essential for safe and effective mRNA products

Defined by WHO as a hazardous byproduct that must be removed

Currently mitigated via expensive and complex purification methods

Increased regulatory scrutiny and QC issue

Linea™ IVT

Two Next Generation Technologies for Better mRNA

Linea™ RNAP polymerase

- Secured via acquisition of Spindle Bio Inc. in July 2023
- Proprietary fusion enzyme comprised of a high fidelity RNAP and DNA binding domain
- Chemically binds to Linea™ DNA IVT templates allowing unique IVT conditions that reduce or mitigate dsRNA
- No impact on RNA fidelity
- Pending IP in over 15 countries

Linea™ DNA IVT Templates

- Leverages platform advantages for 100% enzymatic production of IVT templates
- Reduces up to 40% of the IVT steps used to manufacture mRNA
- Homopolymers are added enzymatically providing homogeneous poly(a) sequence in mRNA
- Chemical modification needed to enable Linea RNAP easily added

Linea™ IVT

Simplified mRNA Production

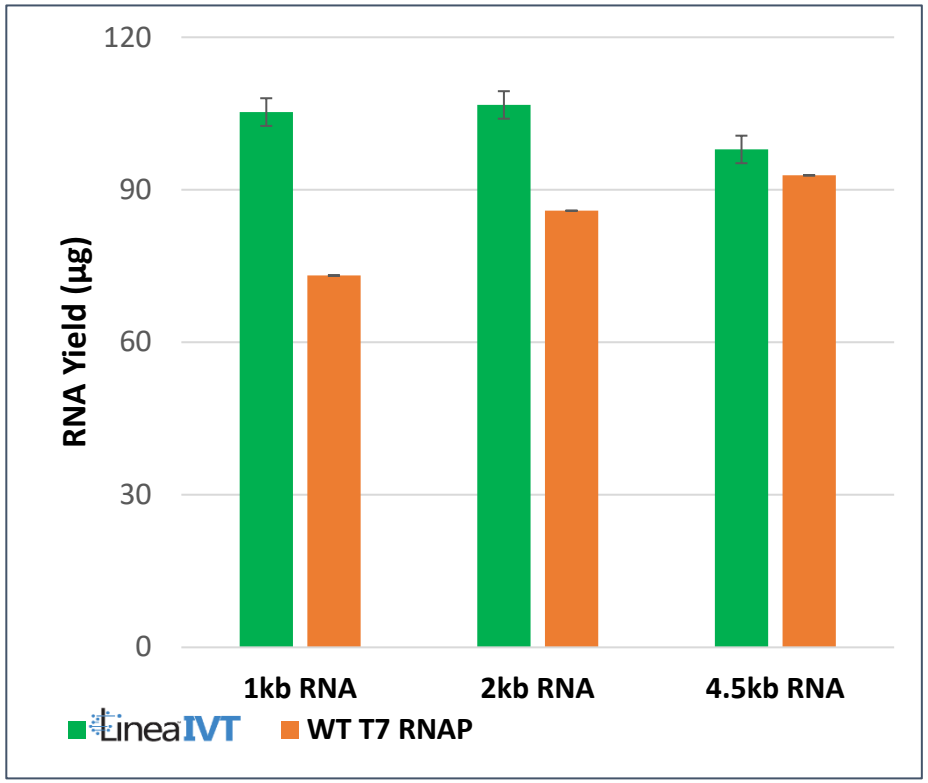
Conventional IVT mRNA Production

Linea™ IVT mRNA Production

Process step reduced or eliminated by Linea™ IVT

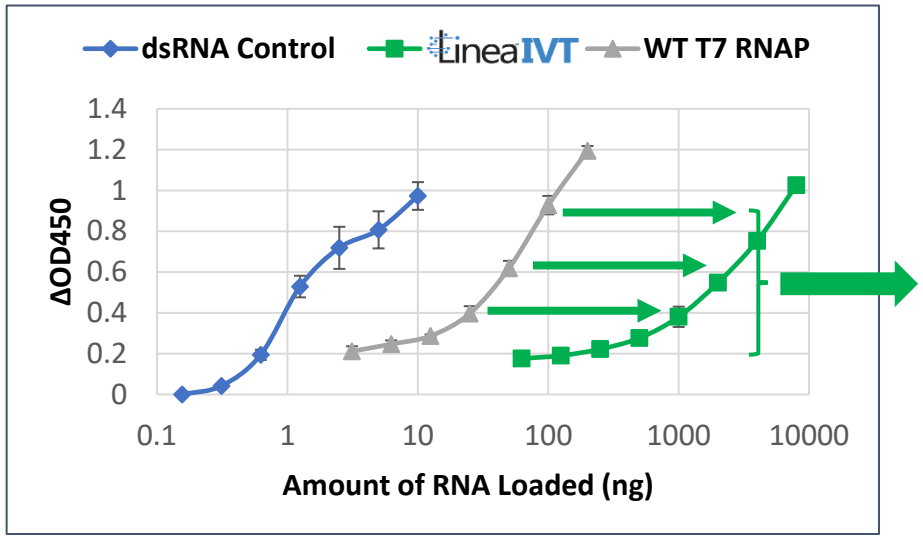
Equal or Greater RNA Yields with Mitigated dsRNA

RNA Yields



- Equal or greater yields than legacy RNA platforms with *up to 50x dsRNA reduction*
- Minimal optimization required for new constructs

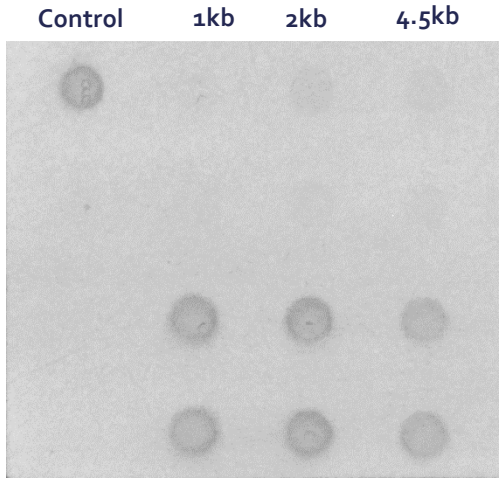
dsRNA by J2 ELISA



LineaIVT ≈50x dsRNA Reduction from WT T7

dsRNA by J2 Dot Blot

Lower dsRNA concentration results in lighter or no dot

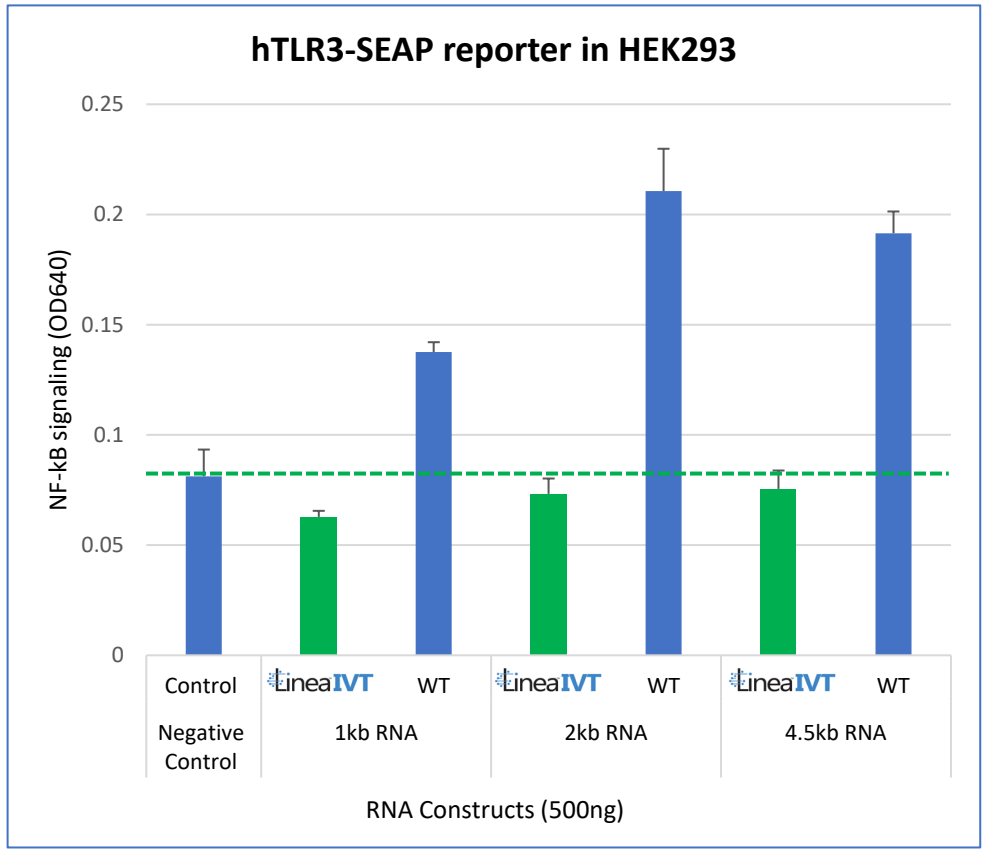


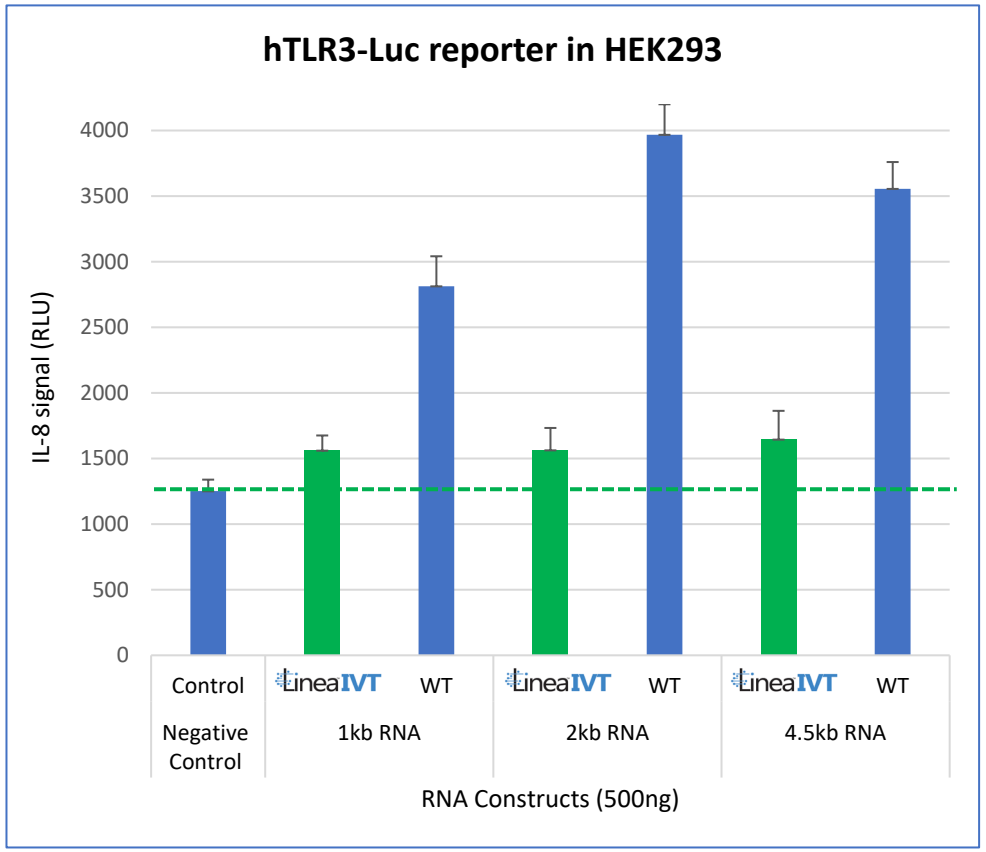
LineaIVT

WT T7 RNAP

Reduced Unwanted Cellular Immune Stimulation

- dsRNA mitigated mRNA produced with Linea™ IVT reduced unwanted cellular immune stimulation *in vitro* to near negative control levels
- mRNA produced with legacy platform showed significant unwanted cellular immune stimulation *in vitro*



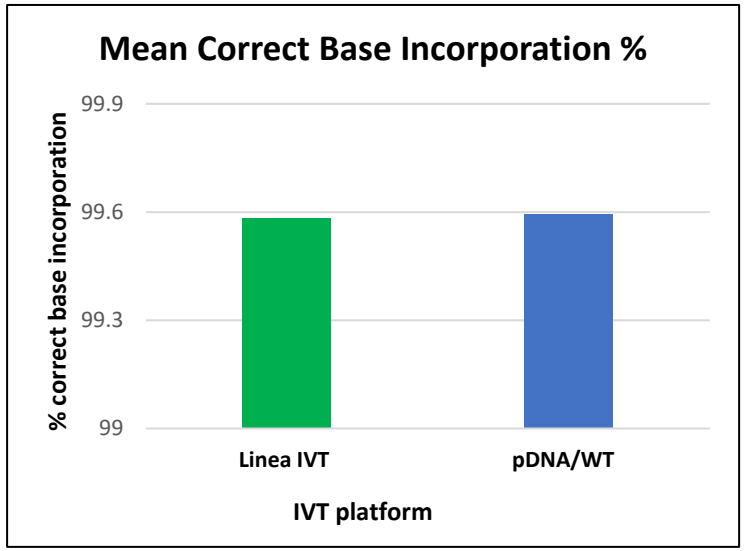


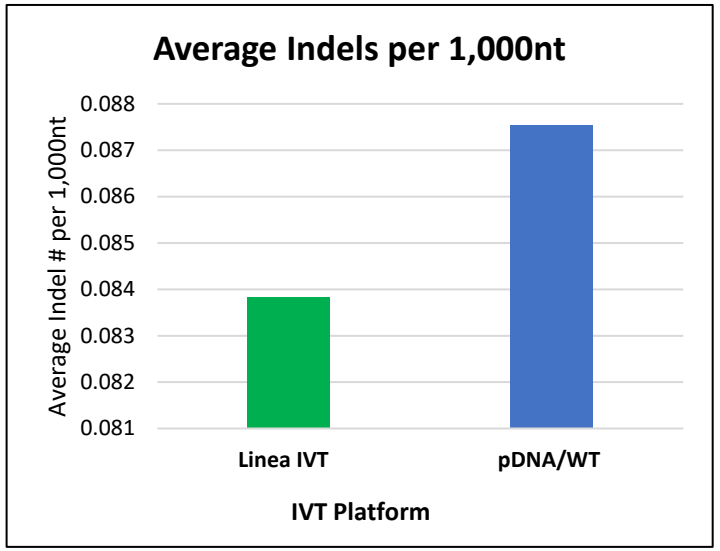
dsRNA Mitigation Without Compromise

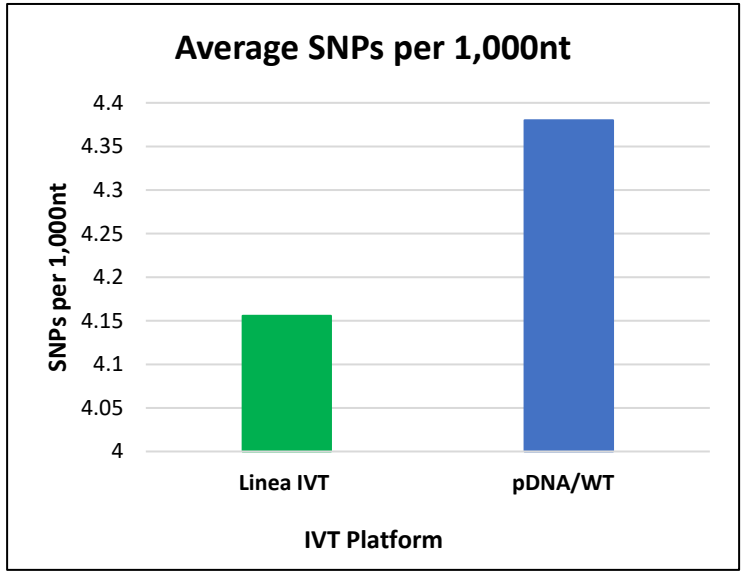
High Fidelity RNA Production

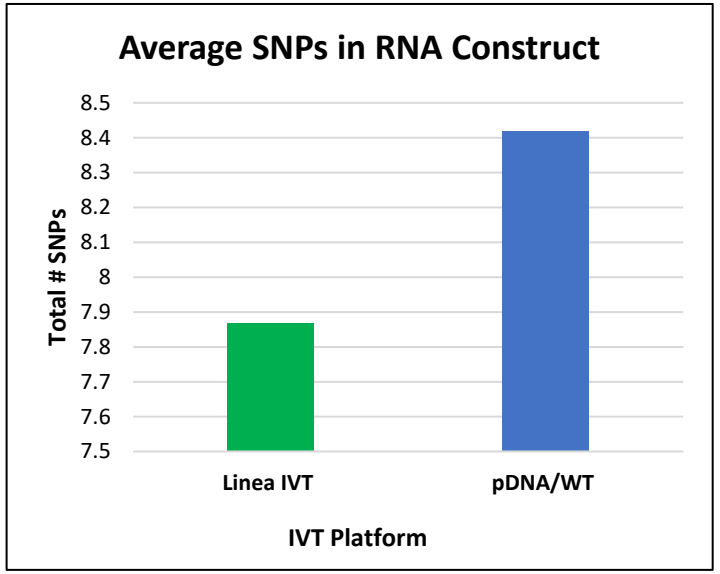
As compared to legacy IVT platforms (pDNA + wild type RNAP):

- Statistically equivalent mean correct base incorporation rate
- Lower average SNP errors
- Lower average Indel errors
- Lower overall SNP error in final RNA construct





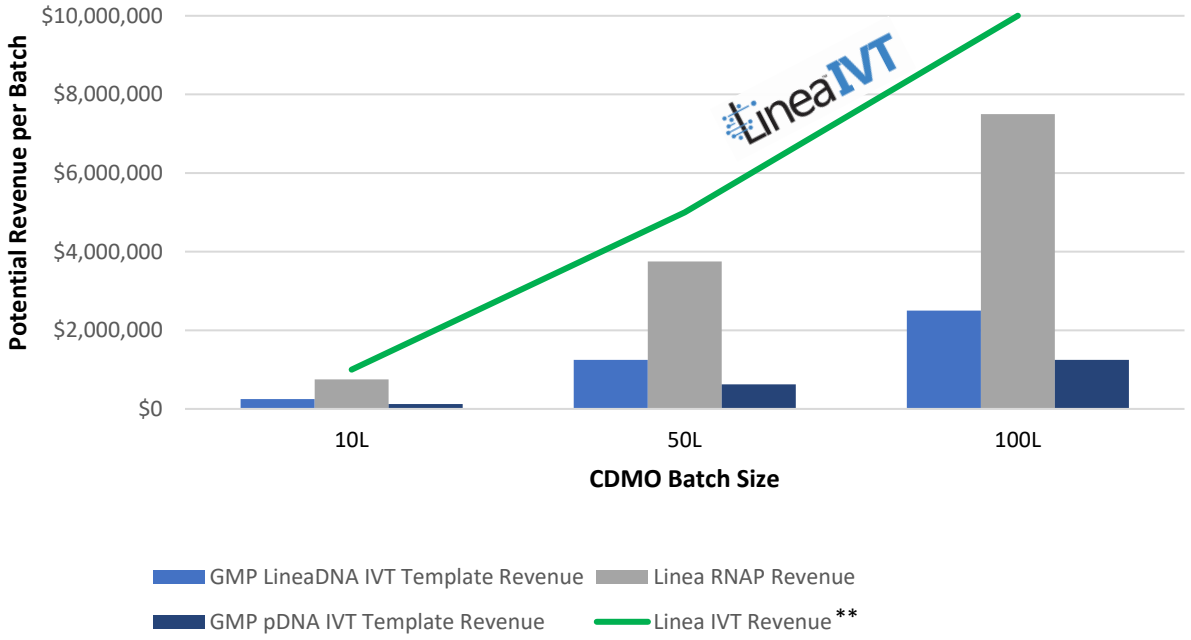




*Error rate and SNP/Indel analysis studies performed via deep read NGS

Capturing More mRNA Manufacturing COGs

Illustrative Linea™ IVT Potential Revenue per Selected mRNA Batch Sizes (10L, 50L and 100L)*



Linea™ DNA is the Key to Unlocking Linea™ RNAP Value

- RNAP is one of the most expensive COGs in mRNA manufacturing
- Linea IVT templates enable the sale of Linea RNAP
- Linea IVT potentially produces ≈3X the revenue opportunity compared to Linea IVT templates alone*
- Linea IVT potentially produces ≈8x the revenue opportunity compared to pDNA IVT templates alone*

*Based on Company Internal Modeling and Current Industry Pricing

** Linea IVT revenue is Linea IVT template revenue + Linea RNAP revenue

Financial Snapshot*

$8.7 Million
Market Cap

64,125 Average 3-month daily share volume

$7.2 Million
Cash/equivalents

13.7 Million
Common shares outstanding

21.4 Million
Fully diluted shares

Capital Stock
Series A Preferred: 10M authorized; 0 issued and outstanding

Series B Preferred: 10M authorized; 0 issued and outstanding

*As of closing price on 01.03.24 and Form 10-K filed on 12/7/23

Thank you!

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