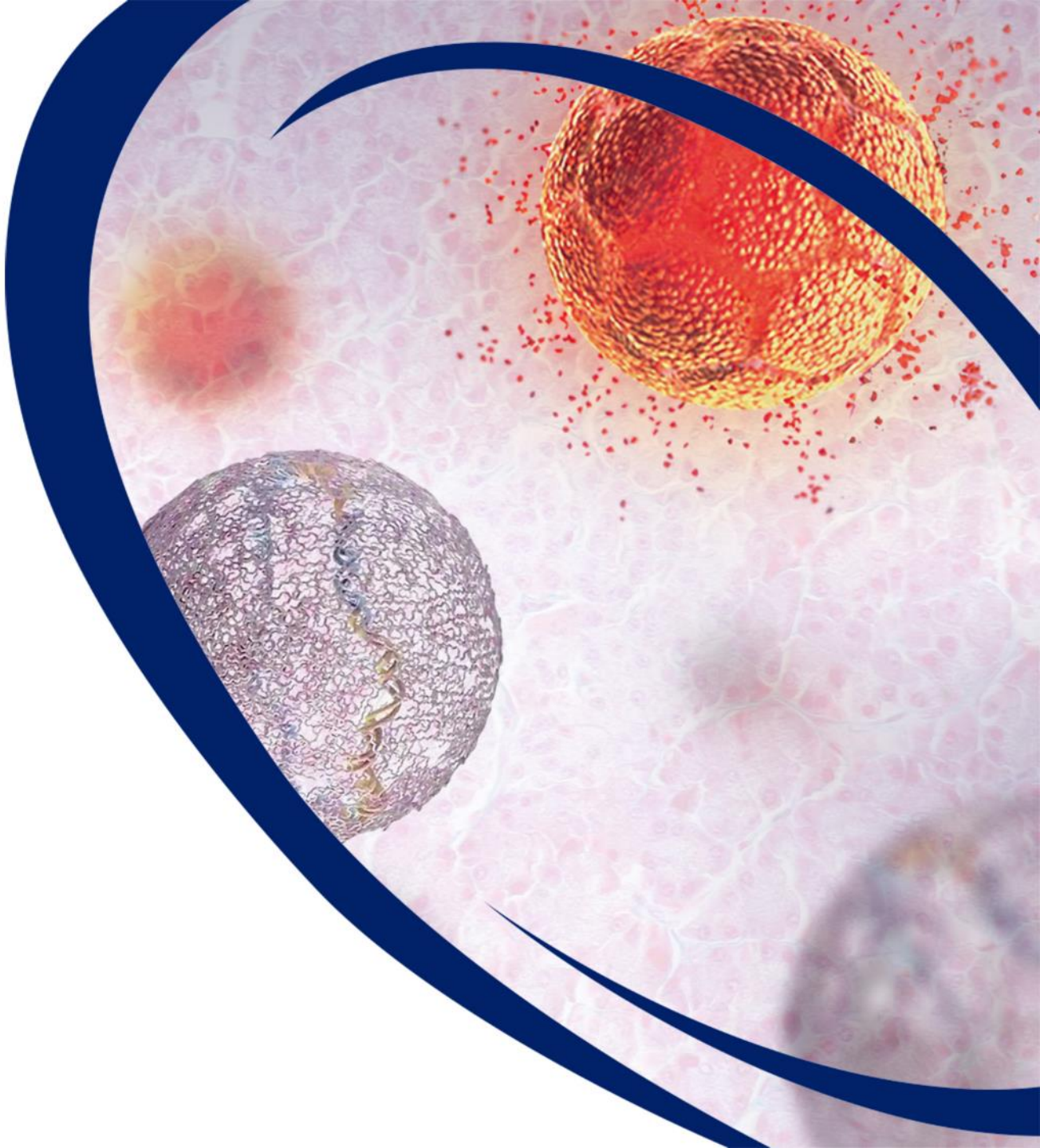
Celsion

Corporate Presentation

Nasdaq: CLSN

June 2022



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While the list of factors presented here is considered representative, no such list should be considered to be a complete statement of all potential risks and uncertainties. Unlisted factors may present significant additional obstacles to the realization of forward-looking statements. Forward-looking statements included herein are made as of the date hereof, and Celsion does not undertake any obligation to update publicly such statements to reflect subsequent events or circumstances except as required by law.

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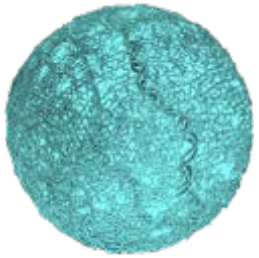
Proprietary DNA Plasmid Technology Platforms

TheraPlas

- Polymeric Nanoparticle Delivers DNA Plasmids Coding for Therapeutic Proteins
- Safely Administered to Over 100 Patients To-Date

GEN-1 Immunotherapy

Localized Interleukin -12 Immunotherapy



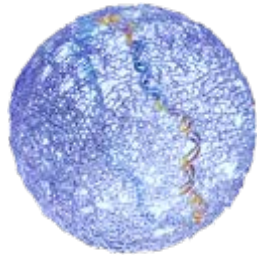
Phase II Evaluation in Advanced Ovarian Cancer
Orphan Drug Designation: U.S. and EU
Fast Track Designation

PLACCINE

- DNA Plasmid vectors engineered for next generation vaccine technology
- Designed for multiple antigens
- Option for the co-expression of immunomodulators

SARS-CoV-2

Multivalent Vaccine for COVID-19



Proof-of-Concept to Demonstrate PLACCINE
as Best-in-Class Vaccine Platform Using
SARS-CoV-2 as a Benchmark

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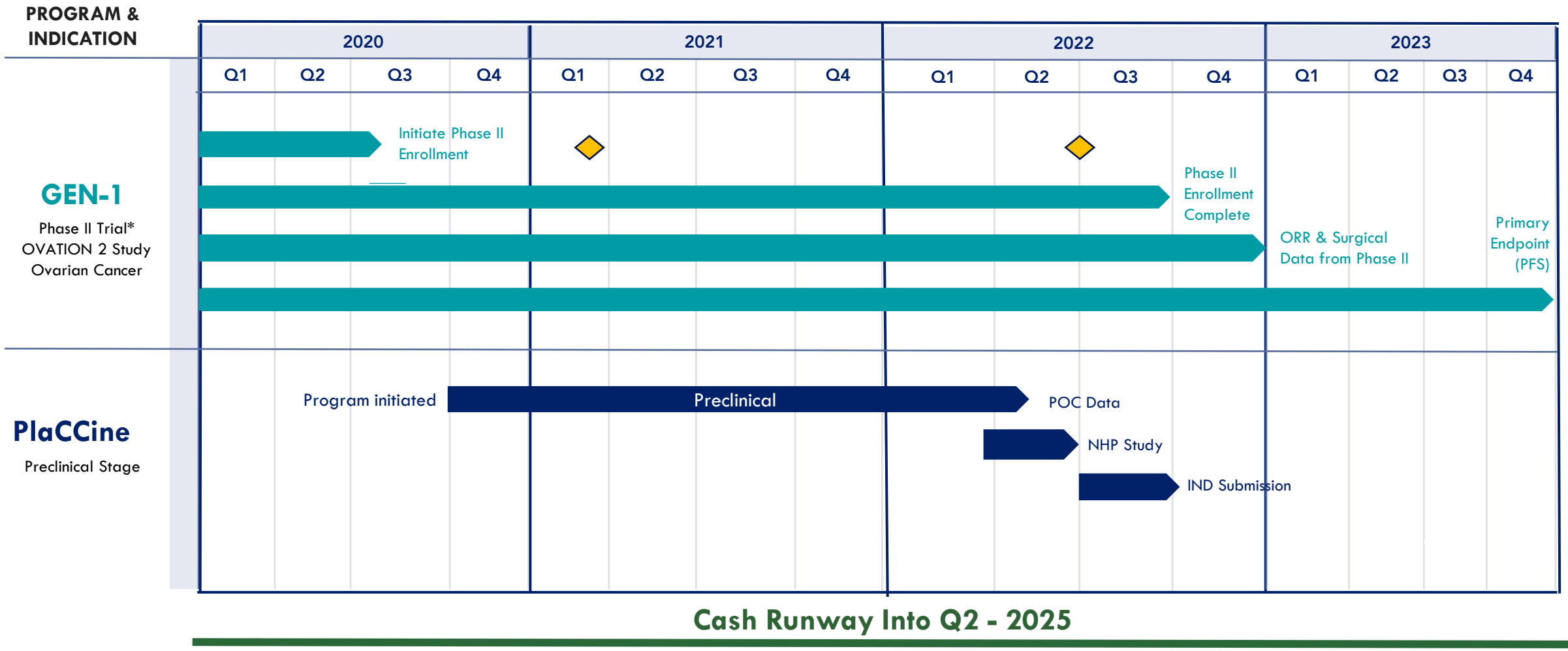
Pipeline Milestone Events
2022 - 2023



Open-label design allows for periodic reporting of results

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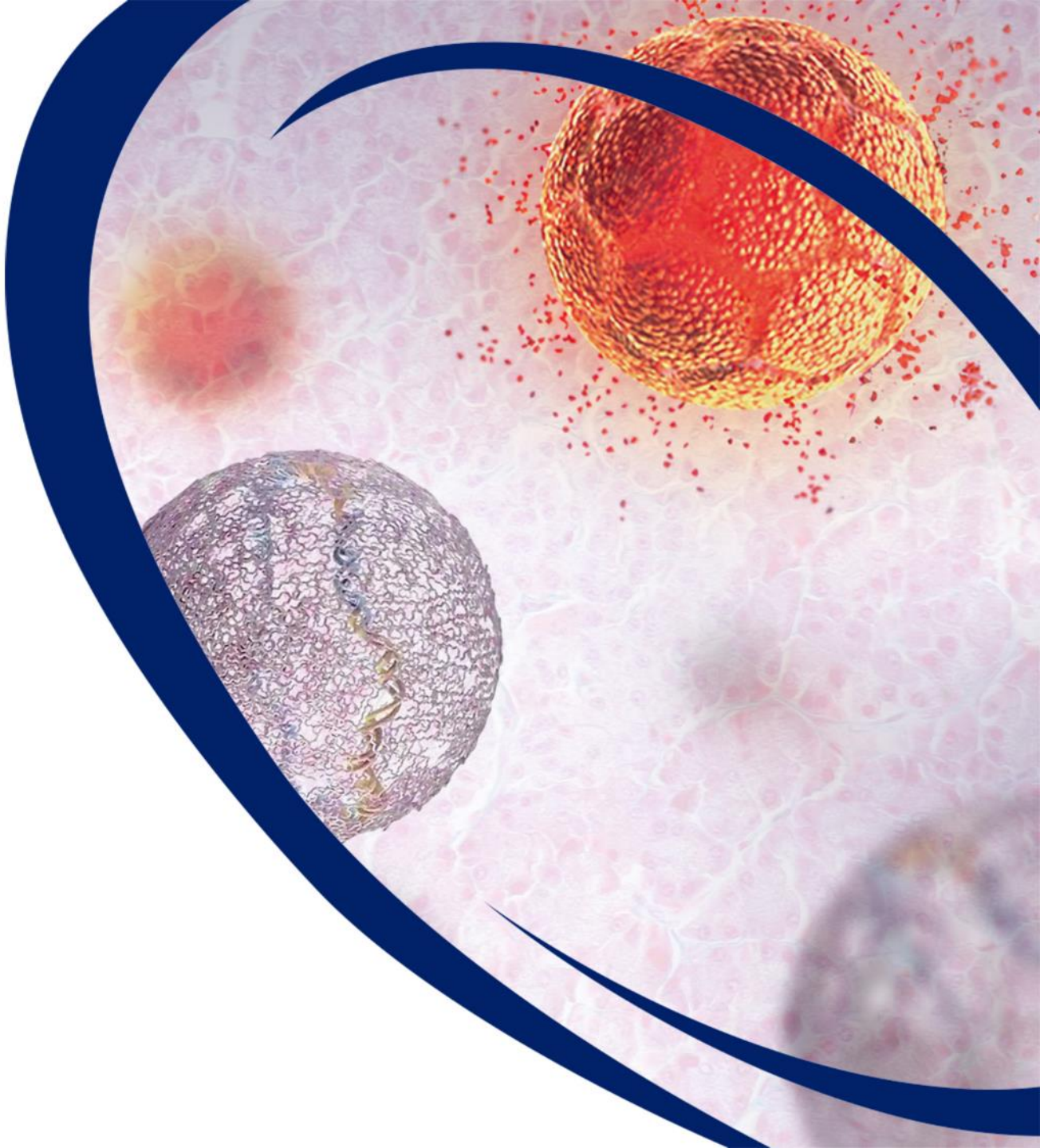
GEN-1 IL-12

IMMUNO-ONCOLOGY PROGRAM



IL-12: A Powerful Immune-Modulating Agent

Interleukin-12 Can Induce Anti-cancer Immunity Through Multiple Mechanisms

Activation/Proliferation

Maturation/Proliferation

Anti-Angiogenesis

Inhibition of Immune Suppression

1 Stimulates the proliferation of CD-8 positive T-cells and natural killer (NK) cells and their cytotoxic activity against the tumor

2 Shifts the differentiation of naive CD-4 positive T-cells toward a TH-1 phenotype, further enhancing the immune response – Turns "cold" tumors into "hot" tumors

3 Promotes cellular production of the potent immune mediator IFN-γ and TNF-α. IFN-γ promotes the expression of anti-angiogenic molecules, halting the growth of new blood vessels that supply oxygen to the tumor

4 IL-12 inhibits regulatory T-cells that suppress immune responses by "hiding" the tumor from the body's immune system

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GEN-1 Composition

Three Component Delivery System of **P**olyethylene Glycol (PEG) **P**olyethyleneimine (PEI) **C**holesterol Combined with IL-12 DNA Plasmid

PEI

Condenses DNA strands into nanoparticles

PEG

Improves stability and protects plasmid from degradation

Cholesterol

Facilitates uptake and trafficking across cell membranes

CMV

CMV

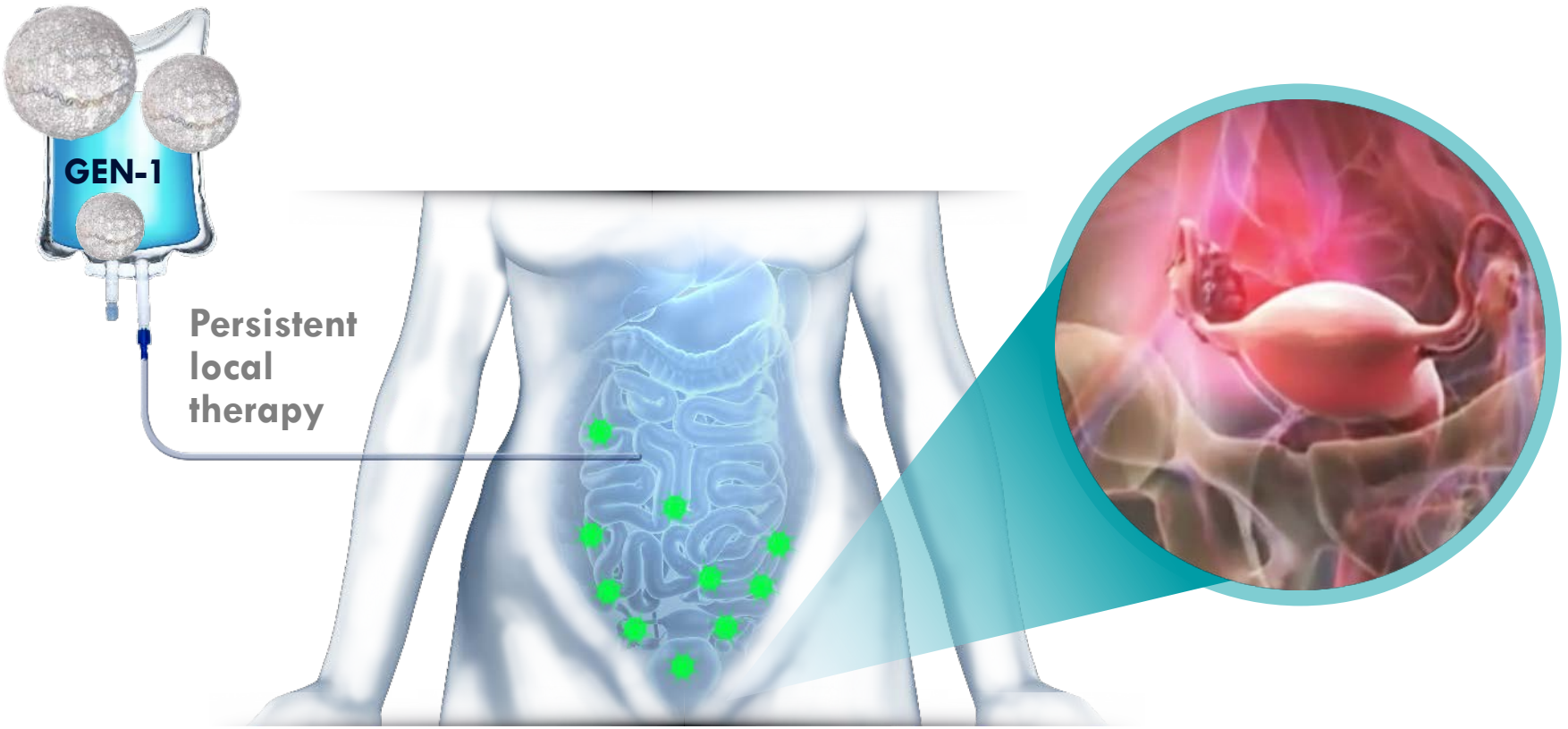
IL-12 plasmid vector

IL-12 plasmid vector carries IL-12 gene and elements for gene expression

GEN-1
Nanoparticles
~150 nm

With intraperitoneal delivery, transfected cells are able to produce sustained concentrations of IL-12 protein in the vicinity of the tumor

GEN-1 Targets Ovarian Cancer Metastases Throughout the Peritoneal Cavity



Local Expression of IL-12 Favors Immune Modulation in Tumor Microenvironment

Intracavity infusion of GEN-1 has demonstrated durable and local expression of IL-12 in the peritoneum

Peritoneal-plasma barrier minimizes systemic exposure of IL-12, thereby giving a favorable safety profile to GEN-1

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Treatment Options in Advanced Ovarian Cancer Are Limited

Recurrence Rates are High and Survival Rates Low

75% of Incidence: Stage III/IV

1st Line

GEN-1 + **Treatment Naïve Population**
Platinum/Taxane Pre and Post Surgery
PFS 12 months | OS 36 months

2nd Line

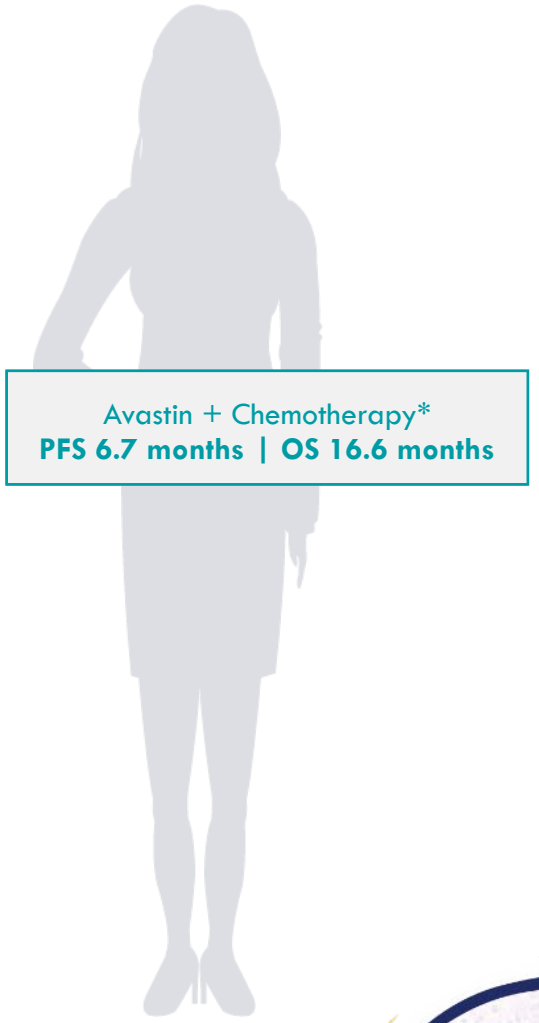
- Platinum Sensitive → Platinum Resistant
- Platinum Resistant
- Platinum Refractory

Avastin + Chemotherapy*
PFS 6.7 months | OS 16.6 months

Treatment - Failed Population

3rd Line

Best Care
OS < 6 months



*Aurelia Trial.

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OVATION I Ovarian Cancer Study

Phase I to Determine Dose, Efficacy, and Biological Activity With NAC in Stage III/IV Patients

Newly Diagnosed
Ovarian Cancer
Tissue Collection

Standard Neoadjuvant
Chemotherapy (NAC) +
8 weekly cycles of GEN-1

Interval Debulking
Surgery
Tissue Collection

Ovarian Cancer Patients
(FIGO IIIC & IV)

3 + 3 Dose Escalation
Starting at 36 mg/m²

Final Dose at 79 mg/m²
6 patients

Primary Endpoint

Safety

Optimal Dose

Secondary Endpoints

Clinical Response, PFS
Pathological Response,
Surgical Response,
Biological Response

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OVATION I Study

Clinical and Molecular Dose Dependent Responses Observed

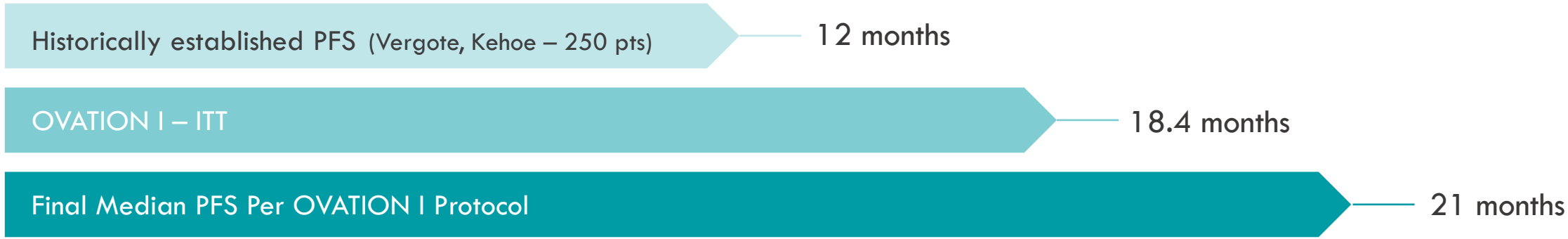
Clinical Responses*

	GEN-1	
	Low-Dose Cohorts 36 mg/mg² & 47 mg/mg²	High-Dose Cohorts 61 mg/mg² & 79 mg/mg²
Objective Tumor Response (CR/PR) RECIST 1.1	66%	100%
Interval Debulking Status R0 Resection Rate	33%	88%
Chemotherapy Response Score CRS 3 Rate	17%	50%

* Chemotherapy dose consistent across all GEN-1 dosing cohorts

OVATION I: Improved Progression-Free Survival Demonstrated with GEN-1

Improvements vs Medidata Synthetic Control Arm in Comparable Patient Populations



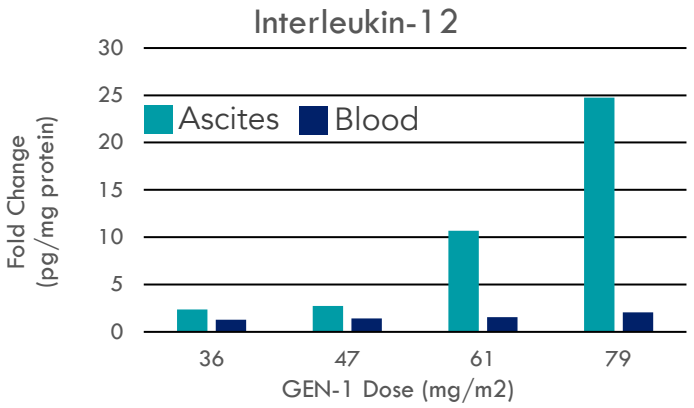
Similar Baseline Patient Characteristics in the OVATION I Study vs Medidata Synthetic Control Arm

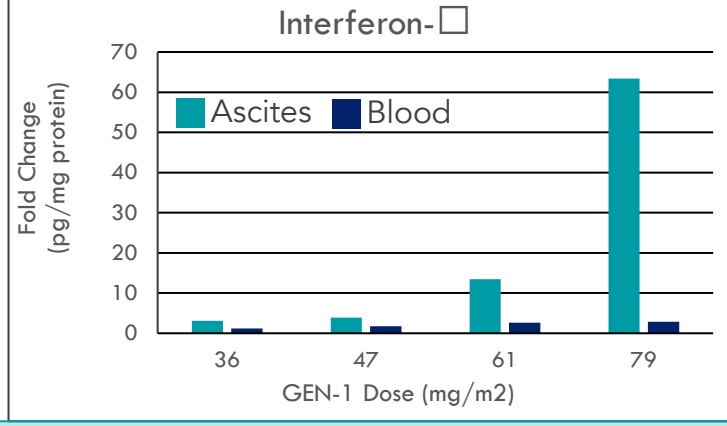
GEN-1 Population	# of Patients	PFS Hazard Ratio	95% Confidence Interval	Log-Rank P-Value
Intent-to-Treat	15	0.53	(0.16, 1.73)	P = 0.29
Per Protocol	13	0.33	(0.08, 1.37)	P = 0.11

OVATION I Study Translational Data Sampling

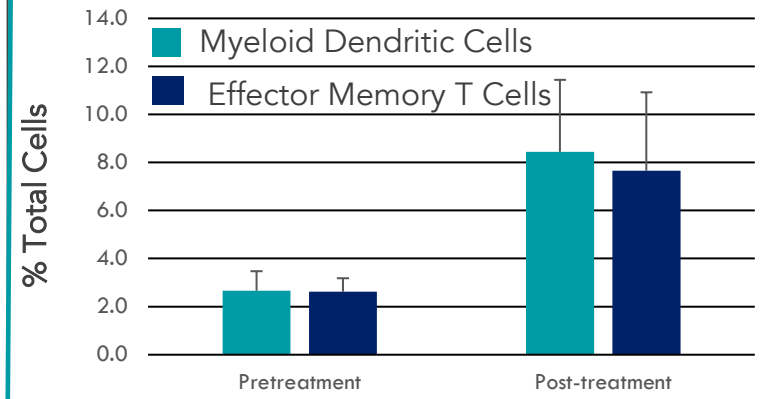
Ascites

Marked Dose-Dependent Increase in Anti-Cancer Cytokine Levels



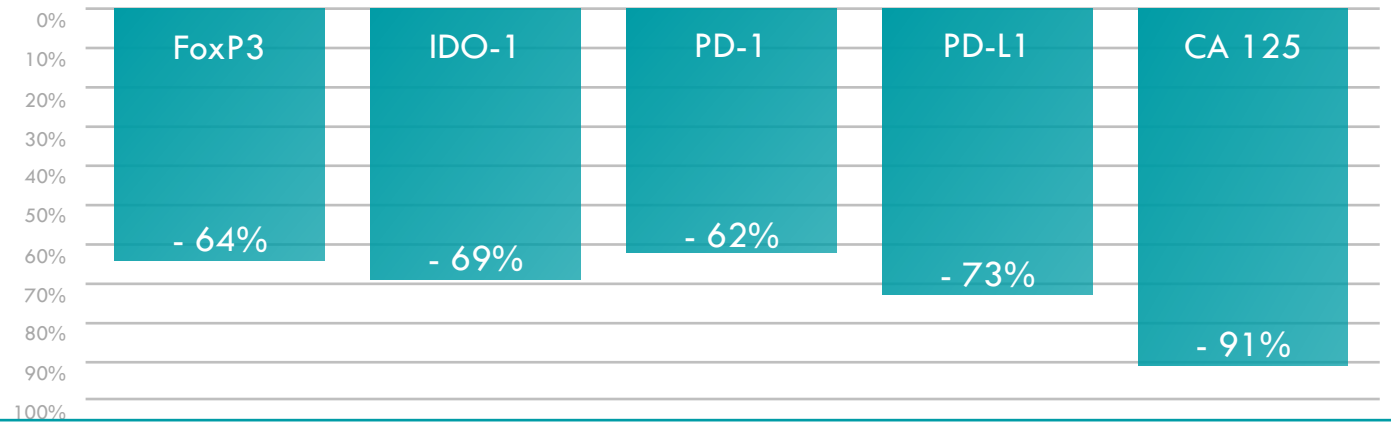


Increase in Dendritic and T_{EM} Cells

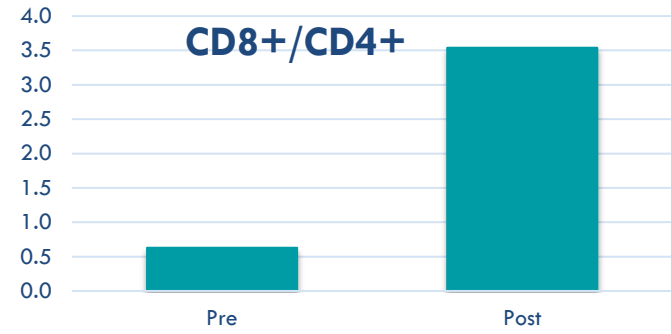


Tumor

Decrease in Immunosuppressive Biomarkers



Increase in CD8+/CD4+ in Tumor



- Increases in cytokine levels shows GEN-1's activity; Low cytokine blood levels underpin the safety profile of GEN-1
- Increase in anti-cancer dendritic cells & effector memory T-cells demonstrate activation of the cellular immune system
- Overall shift in tumor microenvironment to immunostimulatory

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GEN-1 OVATION 2 Ovarian Cancer Study

To Determine Efficacy and Biological Activity With NAC in Stage III/IV Patients

Newly Diagnosed Ovarian Cancer Tissue Collection

1 : 1 Randomization Added Control Arm to OVATION 2

Neoadjuvant Chemotherapy (NAC) + 8 weekly cycles of GEN-1

Interval Debulking Surgery Tissue Collection

Adjuvant Chemotherapy + 9 weekly cycles of GEN-1

Additional Treatment Regimen vs. OVATION I Trial Design

Continue GEN-1 treatment following surgery (Maintenance Therapy)

Ovarian Cancer Patients (FIGO IIIC & IV)

Up to 110 patients

14 patients in Phase I Run-in (100 mg/m²);

Up to 96 patients in Phase II

Randomized 1:1 NAC +/- GEN-1

Primary Endpoint

Progression Free Survival (PFS)

After 80 PFS events or at least 16 months, whichever is longer

Secondary Endpoints

- Clinical Response (ORR)
- Pathological Response
- Surgical Resection Scores (R0, R1, R2)
- Biological Response
- Safety

GEN-1 OVATION 2 Ovarian Cancer Study
Phase I/II Open Label Controlled Trial

- Phase I Portion (N=14) Completed
- 100 mg/m² GEN-1 Dose Confirmed
- 22 Clinical Sites in U.S. and Canada
- Enrollment Expected to be Completed in Q3 - 2022

Interim Data	NACT ONLY	NACT + GEN-1
Interval Debulking Surgery (35 IDS) R0 Resection Rate	56%	80%
Median Time to Progression (30 events) Median time on study for non-progressors 10.4 months, both arms	8.4 mos. 13 events	11.6 mos. 17 events
Chemotherapy Response Score of 3	18%	29%

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GEN-1 Registrational Plan

Focus on BRCA negative Sub-Group

HRP (homologous recombination proficient with no BRCA 1/2 mutations)

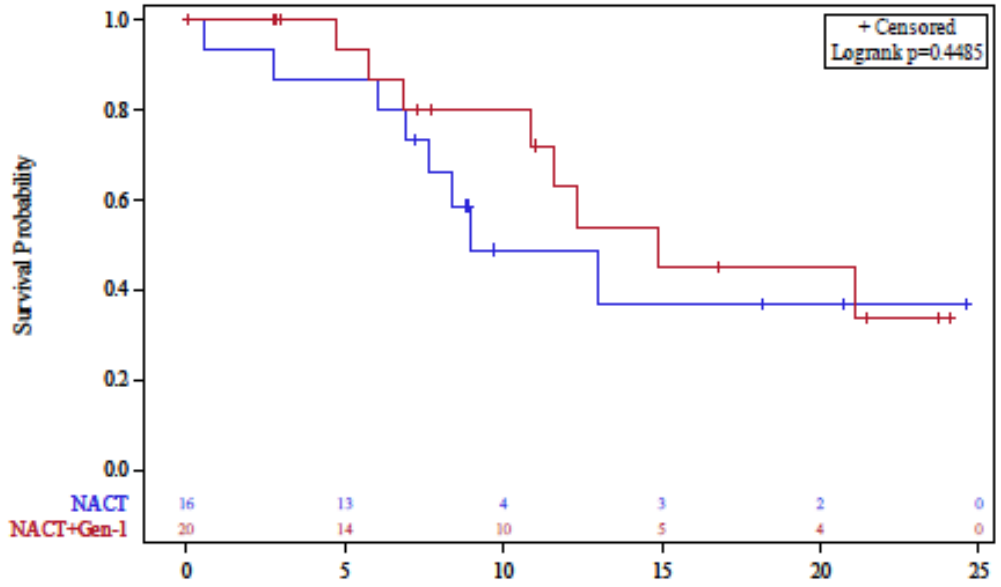
- Median time to progression is about 9 months
- About 45% of ovarian cancer patients are not getting a clinical benefit from PARP inhibitors

Early OVATION 2 data indicates subjects on GEN-1 who are HRP may have improved PFS

- HR 0.68 (95%CI, 0.25-1.85;*P*=0.4511)

Registrational Study to Focus on HRP

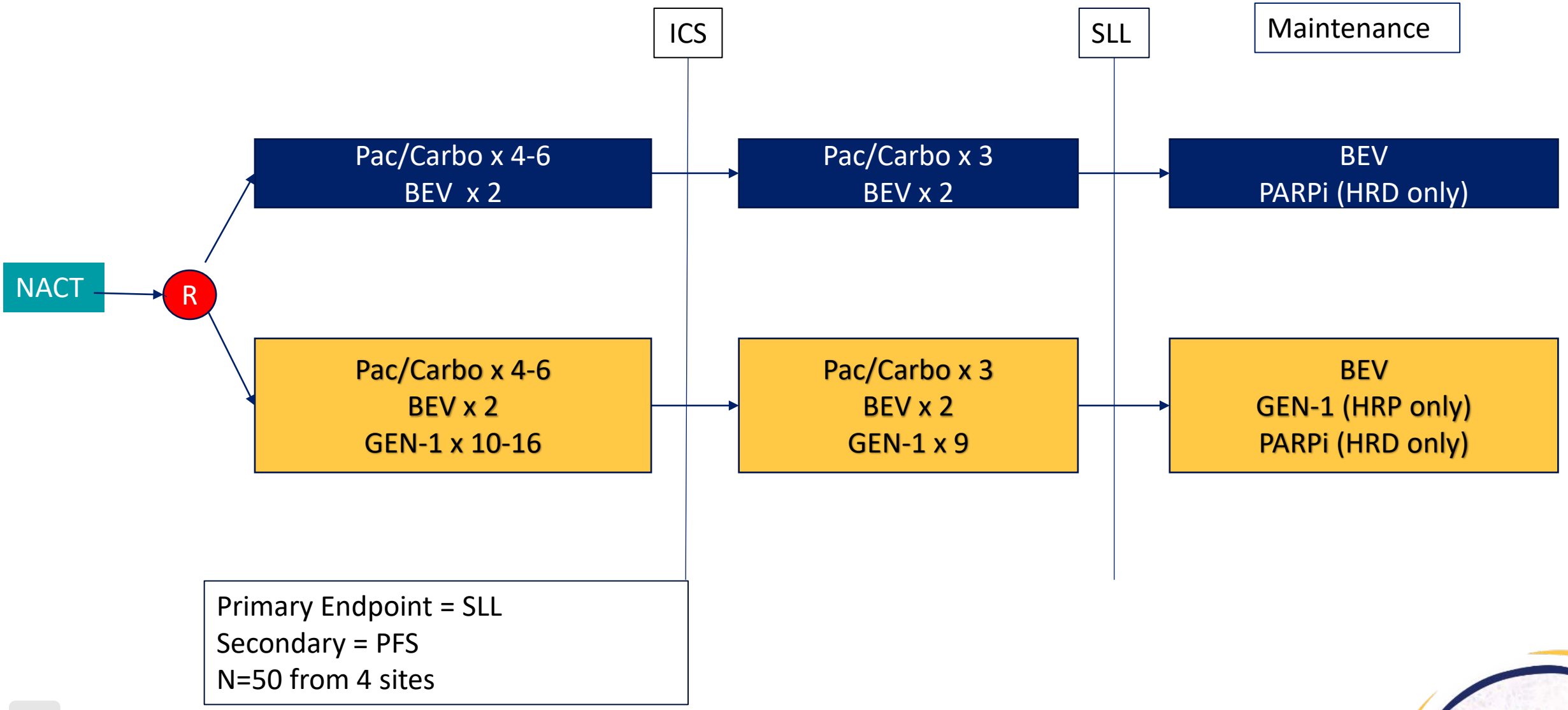
Celsion Study 201-17-201: Analysis of Progression Free Survival Time (Cutoff Date: 19May2022)
Kaplan-Meier Survival Plot and Log-rank Test for BRAC "-" Subjects
Only Subjects with known BRAC status are included



	Subjects	Event	Censored	Median Survival	95% CL	
NACT	16	8	8	9.001	0	0
NACT+Gen-1	20	8	12	14.91	0	0

2nd GEN-1 Study Accepted by FDA

GEN-1 + Avastin (BEV) in Advanced Epithelial Ovarian Cancer



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GEN-1 Summary

GEN-1 offers a novel way to harness the powerful immunological properties of IL-12; The "Master Switch" to the body's immune system

Five completed ovarian cancer trials demonstrate biologic and clinical activity; Strong efficacy signals in Phase I; Mechanism of action confirmed

OVATION 2 offers new hope to a large segment of newly diagnosed advanced ovarian cancer patient population; Phase I portion of OVATION 2 completed in the 2nd quarter of 2020 – Dose for Phase II portion of trial confirmed at 100 mg/m²

Phase II portion of OVATION 2 initiated enrollment in Q3 – 2020 with full enrollment expected to be completed by Q3 - 2022

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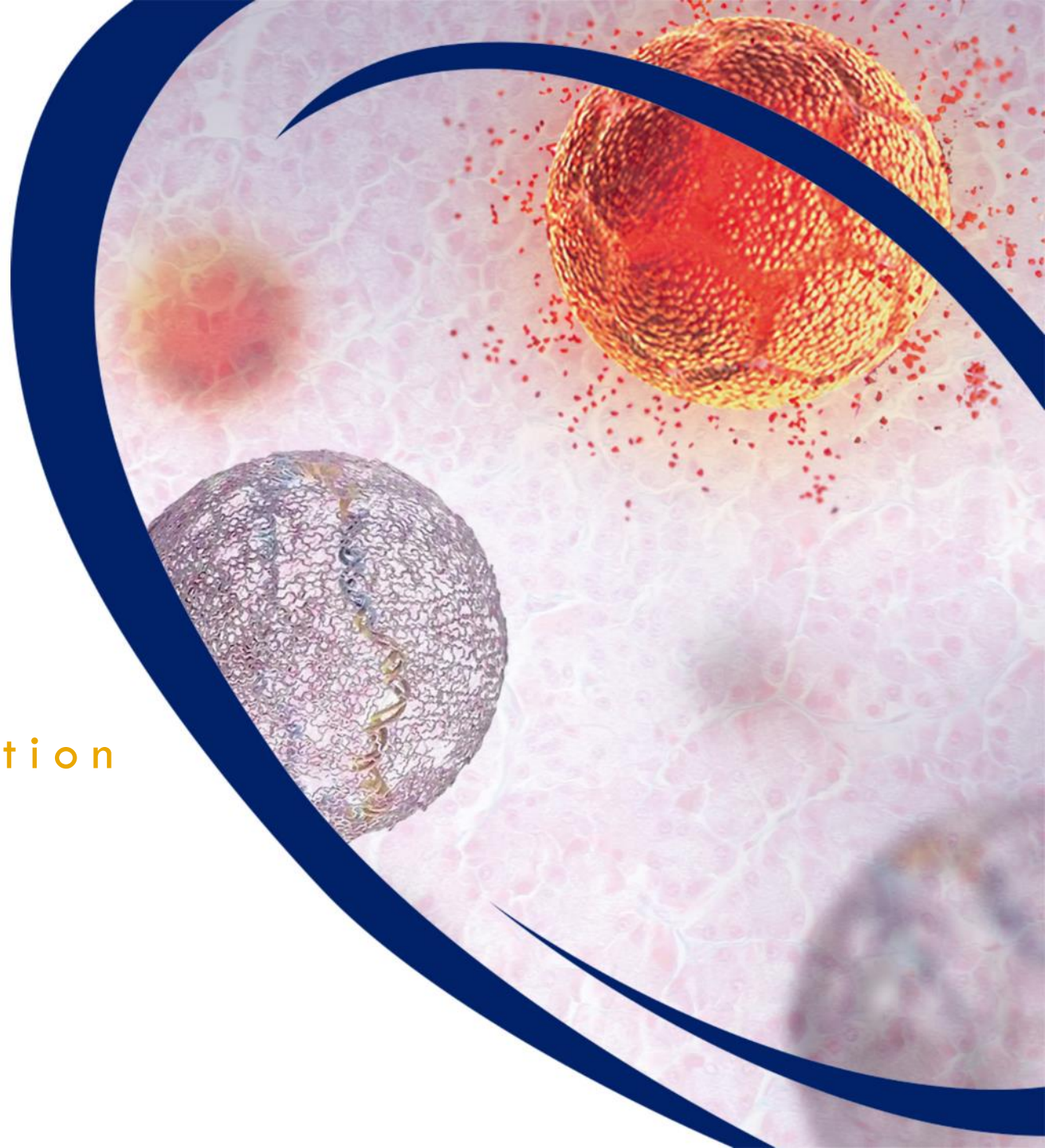
PLACCINE Platform

SARS-CoV-2 Initiative:
Proof of Concept & Validation



PLACCINE* – A Superior Class of Nucleic Acid Vaccine

- We are developing a multivalent pDNA based vaccine platform technology enabling vaccines with superior properties to mRNA vaccines
- Proof of concept is being demonstrated using SARS-CoV-2 vaccines as a benchmark
- Successful results will illustrate superiority to mRNA vaccines in one or more key attributes
- Application of the PLACCINE platform will be valuable in responding to new and existing pathogens with epidemic and pandemic potential

* Patent applications for platform composition and use for both infectious diseases and for cancer vaccines are pending

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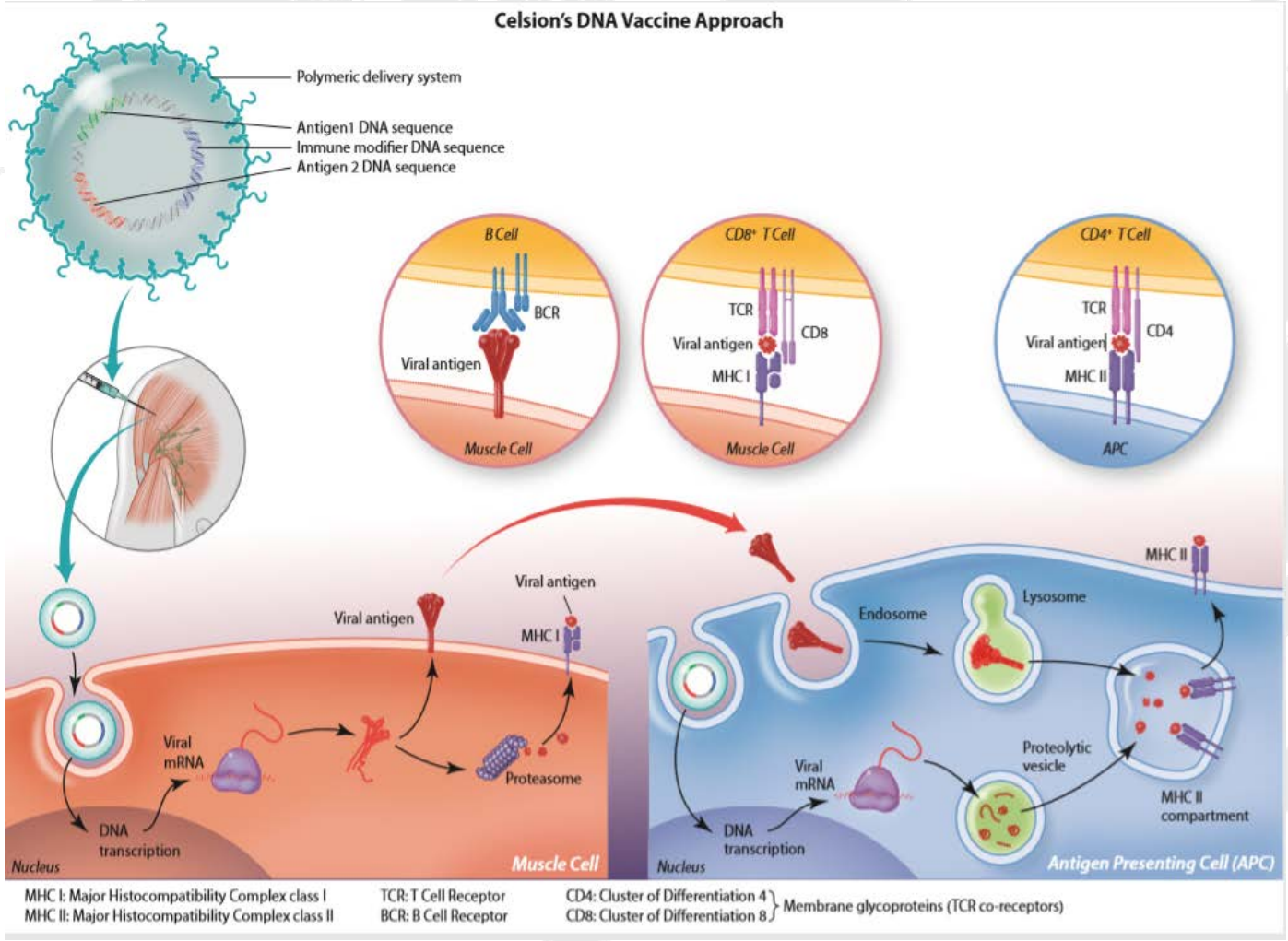
Multivalent DNA Vaccine

Next Generation, based on the Novel PLACCINE Vaccine Platform



PLACCINE Multivalent DNA Vaccine Technology Platform

Single multi-cistronic DNA plasmid vector

- Multiple pathogen antigens
- Potent immune modifier

Delivered with a non-viral, synthetic delivery system

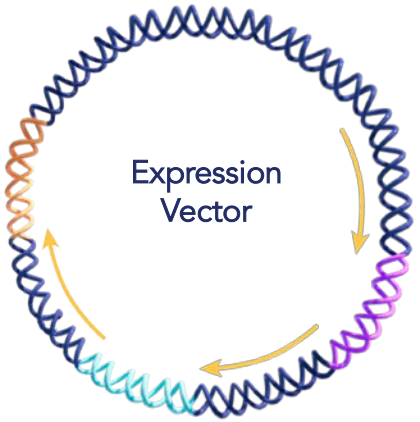
Adaptable for a multitude of pathogens

- Applicable to pandemics
- Infectious diseases that have yet to be effectively addressed

Supported by an established supply chain used for the manufacture of GEN-1

Multi-cistronic Formulated pDNA Vaccine Platform

Proprietary PLACCINE Platform Technologies



- Antigen DNA 1
- Antigen DNA 2
- Optional Immune modifier DNA
- Transcription elements & backbone sequence

Up to 4 antigens have been successfully incorporated and expressed

PLACCINE pDNA System

PLACCINE Delivery Systems

-Synthetic Delivery Systems

- Non-viral
- Non-device

Nanoparticles/Complexes

PLACCINE Vaccines

Intramuscular (IM) Administration

Evaluation of IgG and T-cell responses, Neutralizing antibodies

Potential Administration Routes

- Subcutaneous (SC)
- Intradermal (ID)

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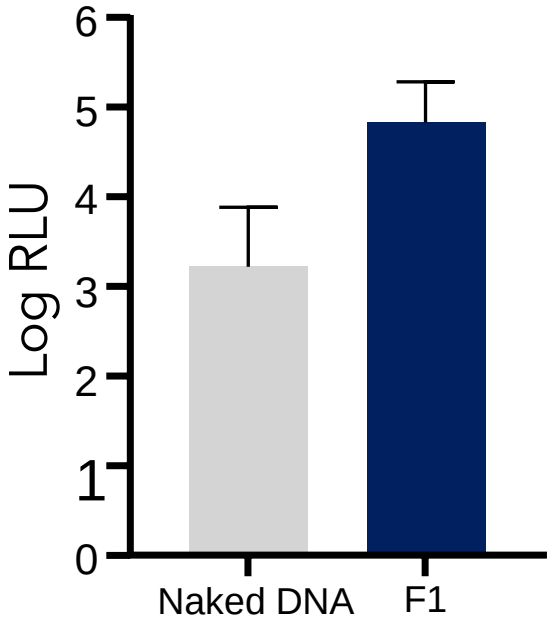
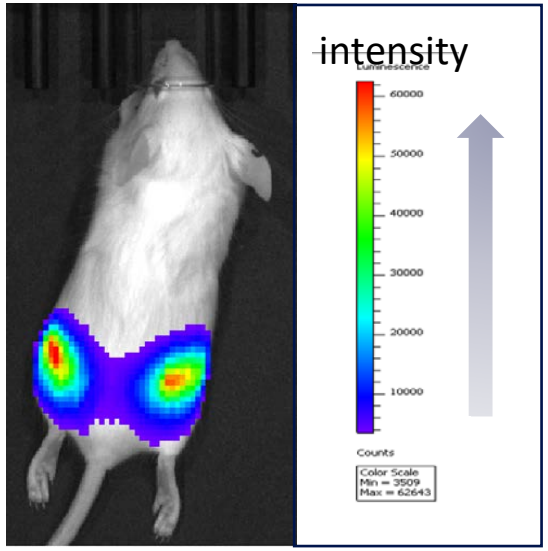
First Generation PLACCINE Formulation F1 Improves Gene Transfer

Forty-fold Improvement Over Naked DNA

- Gene Luciferase
- DNA 25 mg
- Formulation F1, naked DNA
- Expression data Day 1 (RLU), Day 7 (image)

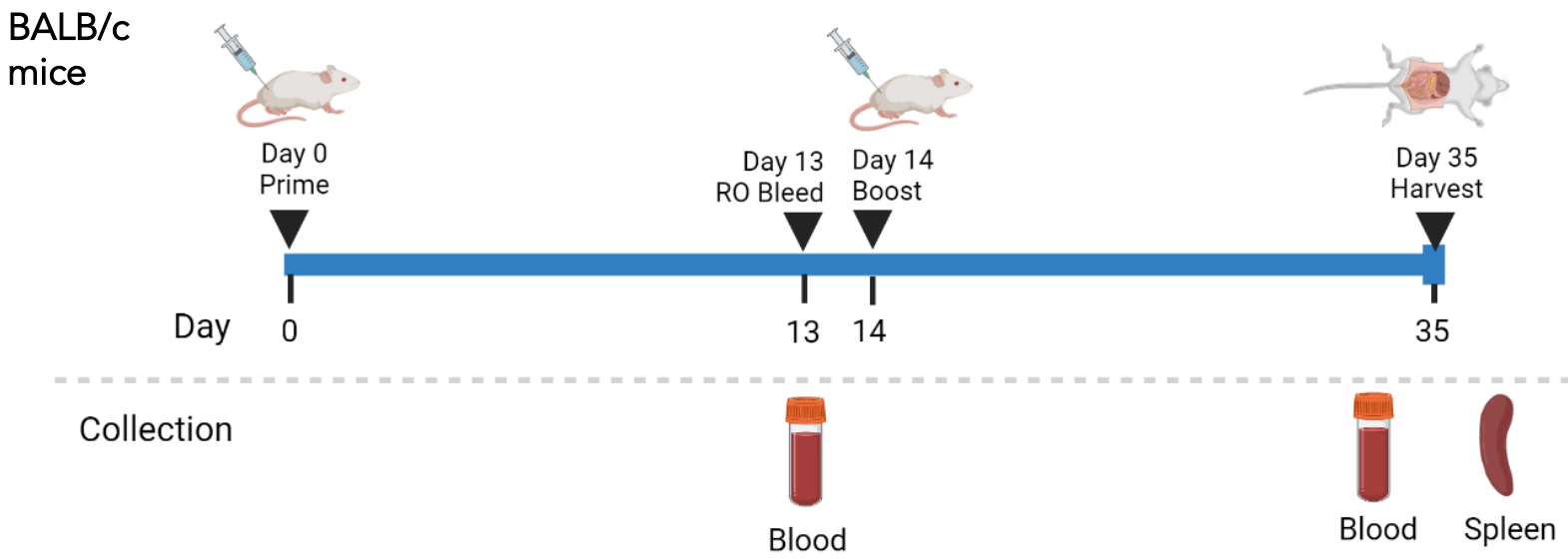




F1

Standard Vaccine Regimen Used For In Vivo Studies

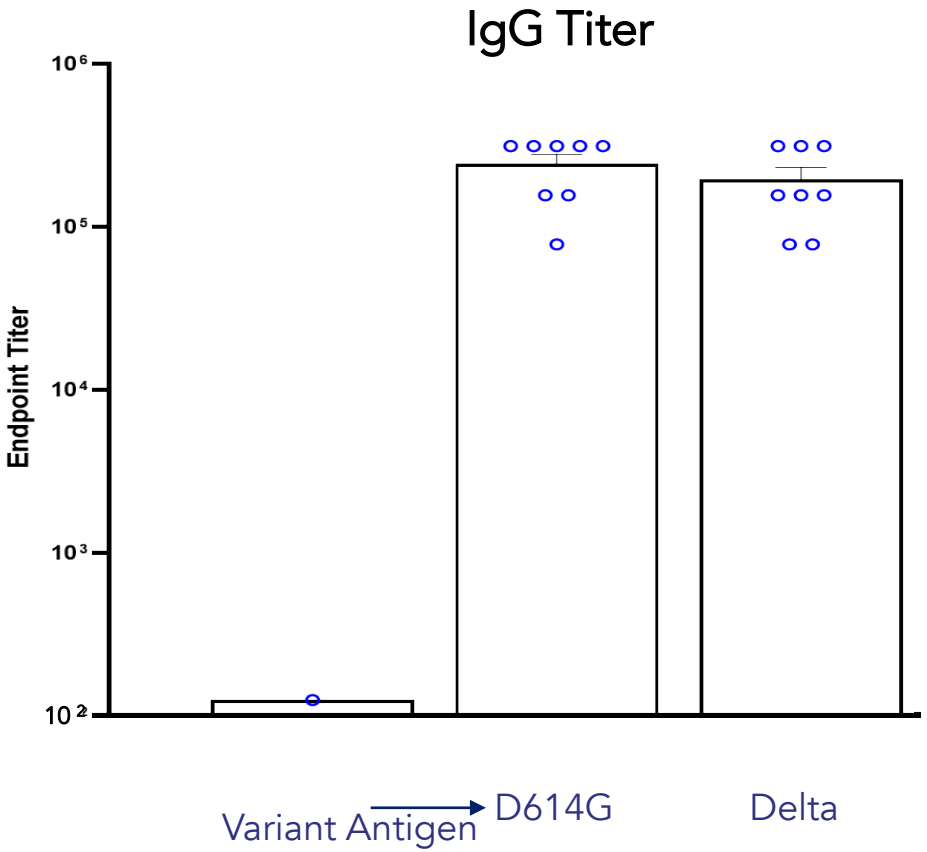
- Prime Day 0
- Bost Day 14
- Bleed for IgG Day 14, 35
- IgG (spleen) Day 35



Latest Vectors Following Optimization of Antigen & Transcription Elements

Single Antigen Vectors - IgG titer

- Optimized vectors pVac-15, pVac-16
- Spike antigen D614G, Delta
- Formulation: F3
- 125 mg DNA
- IgG titer (day 35)

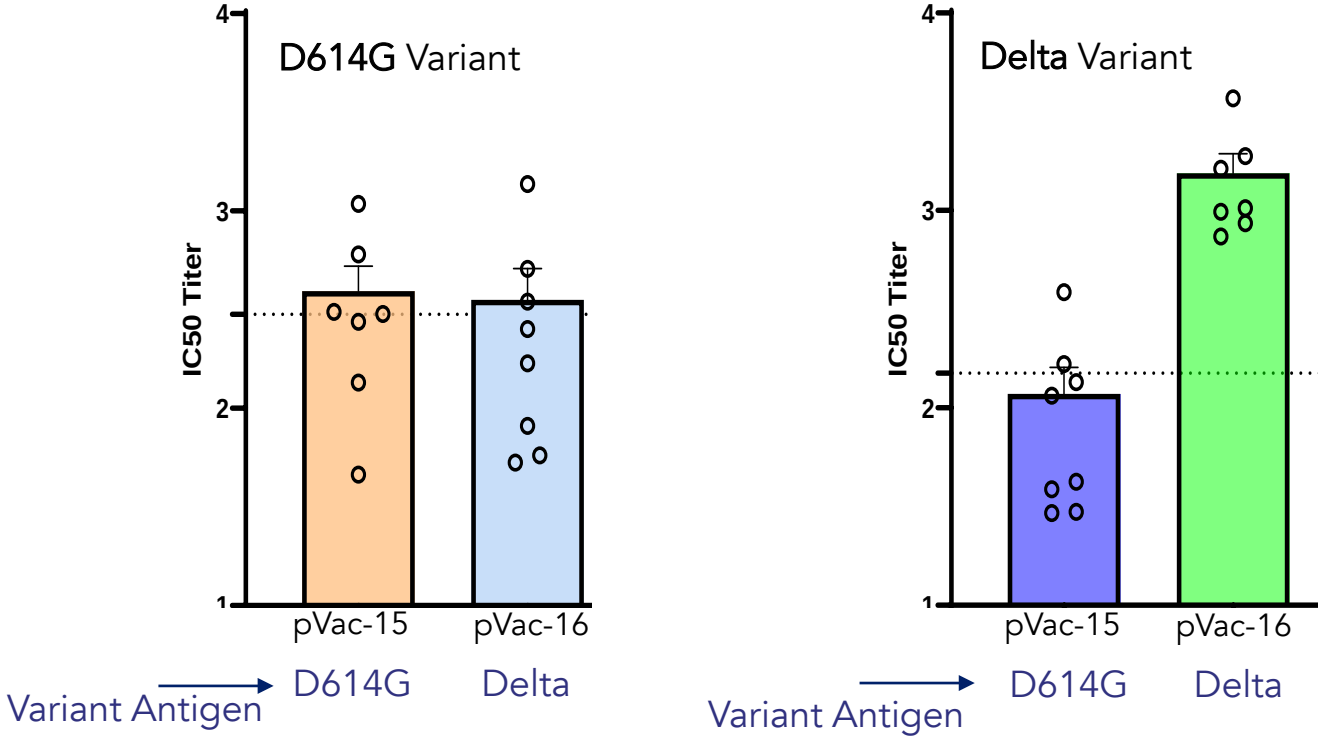


Neutralizing Activity of Latest Vectors in a Pseudoviral Assay

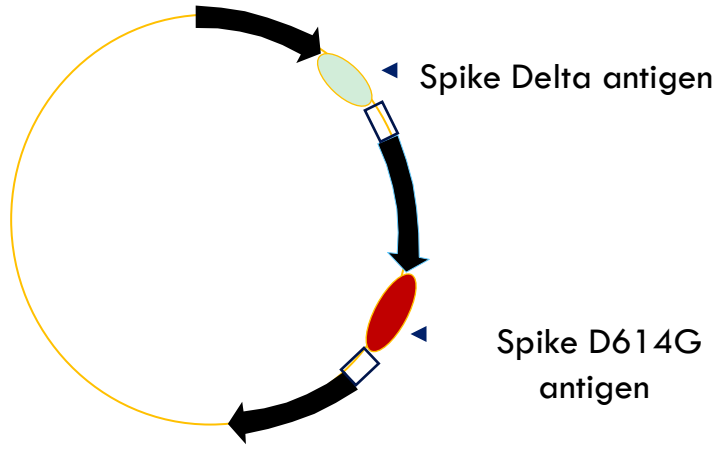
Single Antigen Vectors- nAb titer

- Latest vectors pVac-15, pVac-16
- Spike antigen D614G, Delta
- Formulation: F3
- 125 mg DNA
- IgG titer (day 35)

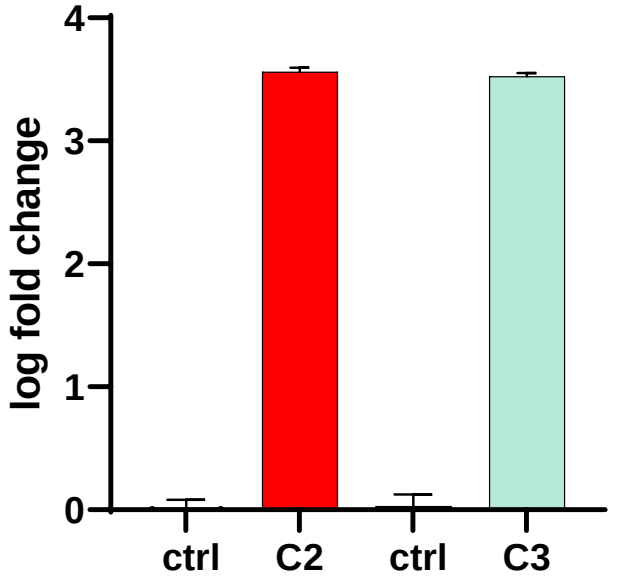
Neutralizing Antibody Titer



Multicistronic Vector Expressing Two SARS-CoV-2 Antigen Variants



Two-Variant Multicistronic Vector



Distinguishing between D614G and Delta by sequence-specific qPCR primers

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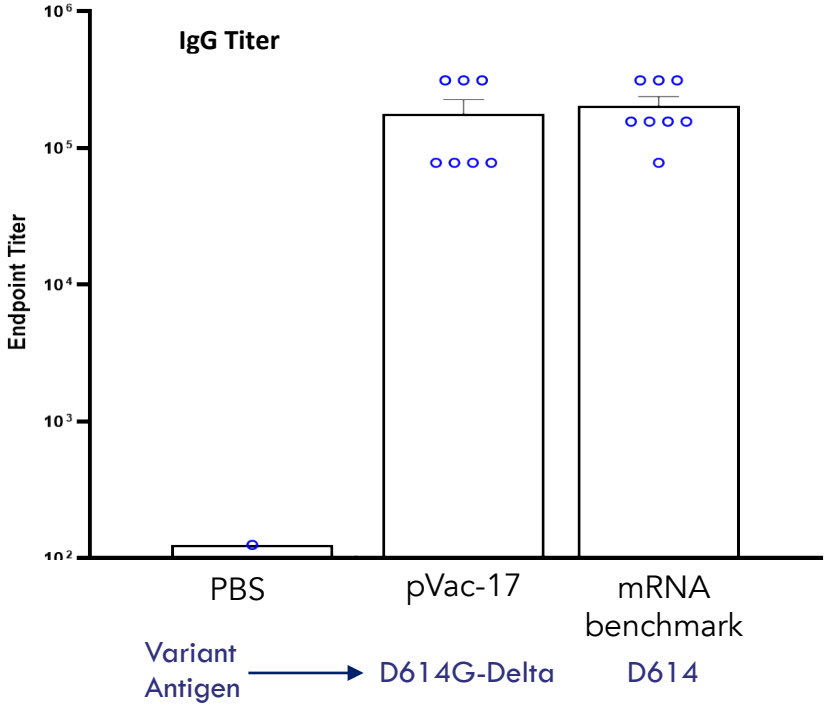
Multicistronic PLACCINE Vaccine Protects Against Multiple Variants

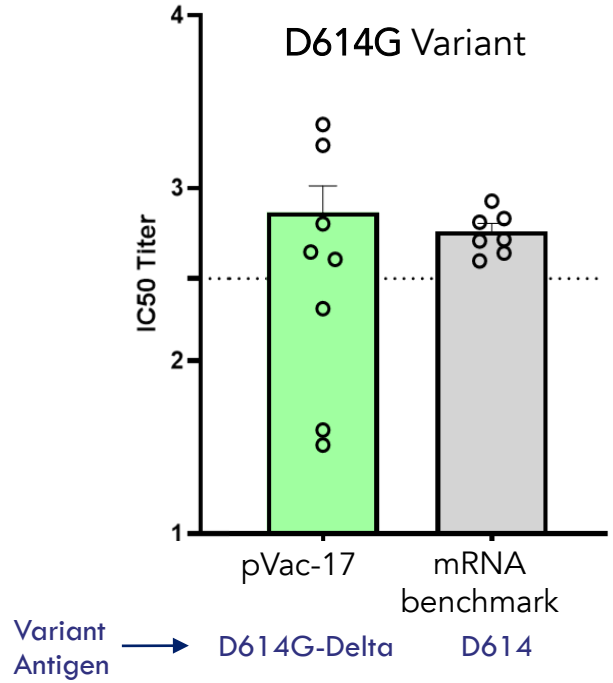
IgG and nAb Titers Comparable to a Commercial mRNA Vaccine

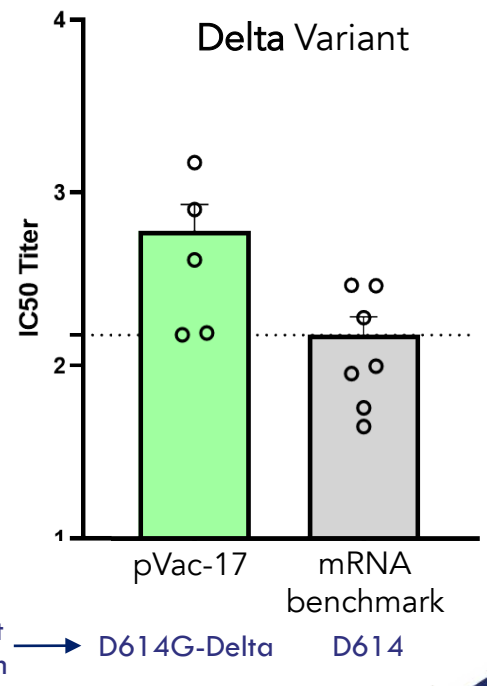
- Multicistronic vector pVac-17
- Spike antigen D614G, Delta
- Formulation: F3
- 125 mg DNA
- IgG titer (day 35)

IgG Titer



Neutralizing Antibody Titer





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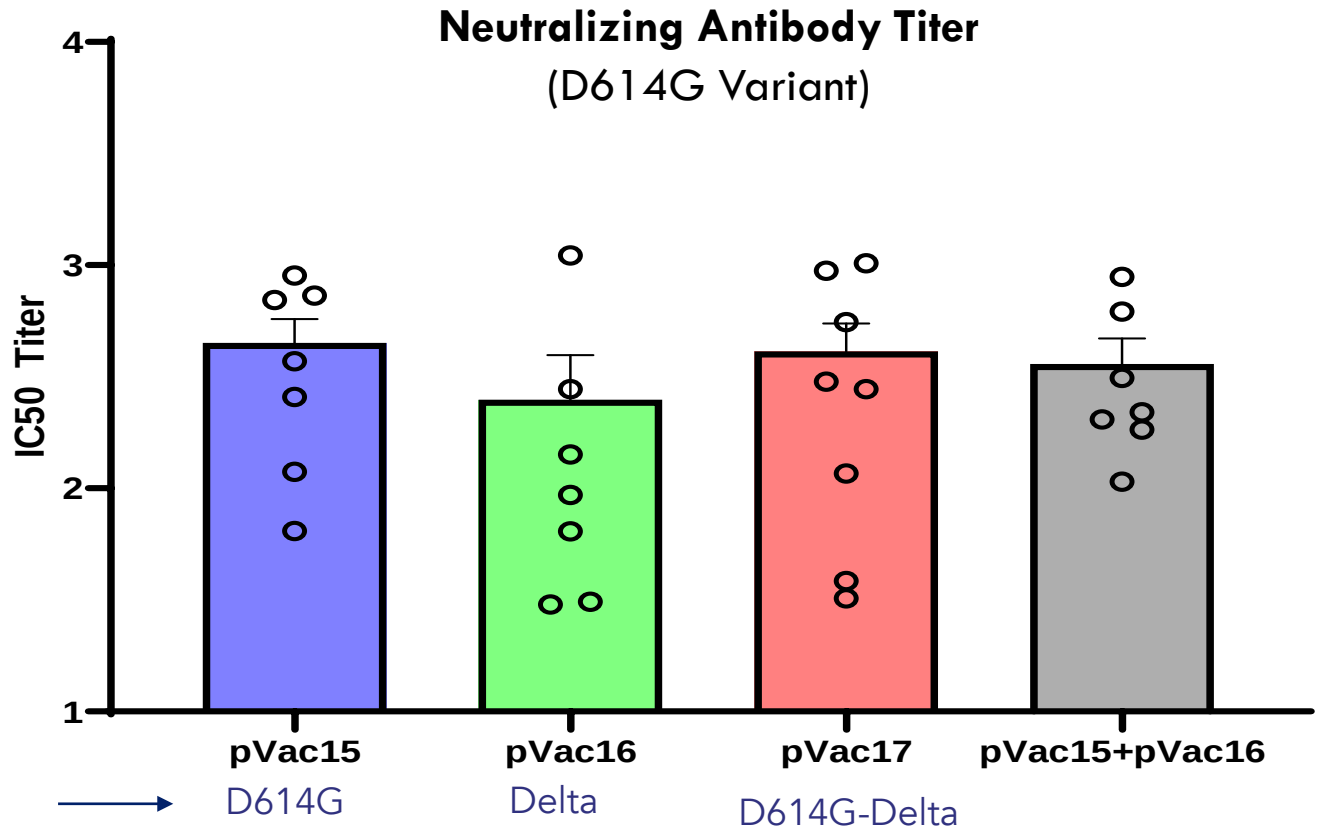
Immunogenicity of Single & Multiple Antigen PLACCINE Vaccines

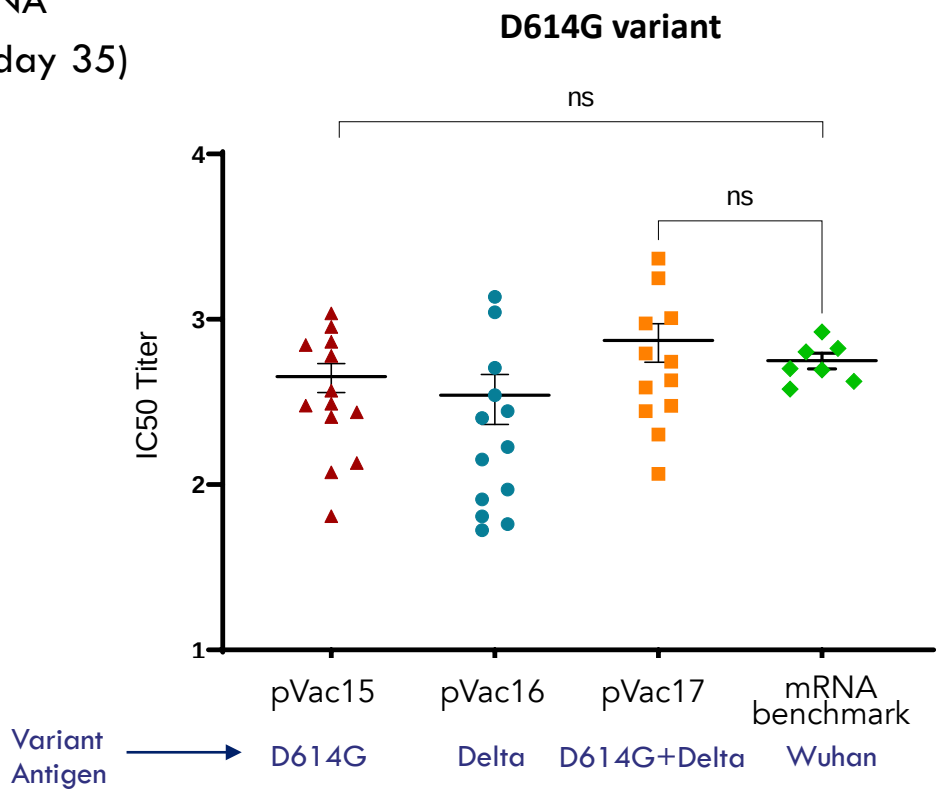
Neutralizing Ab Response to All Vaccine Vectors Observed

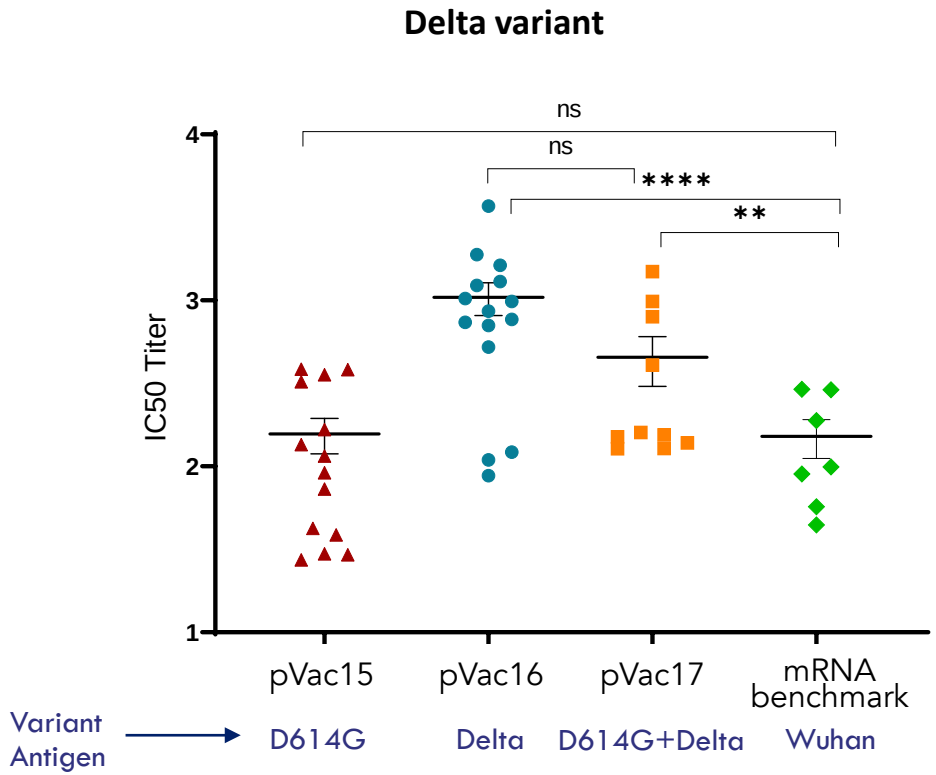
- Vectors: pVac-15 (D614G)
  pVac-16 (Delta)
  pVac-17 (D614G+Delta)
- Formulation: F3
- 125 mg DNA
- IgG titer (day 35)



PLACCINE Bi-cistronic DNA Vaccine Produces Neutralizing Immune Response Against Two Variants

- Vectors: pVac-15 (D614G); pVac-16 (Delta); pVac-17 (D614G+Delta)
- Formulation: F3
- 125 mg DNA
- IgG titer (day 35)





T-test (unpaired, two-tailed)
ns – nonstatistical; * P value < 0.05; ** P value<0.001; *** P value 0.001

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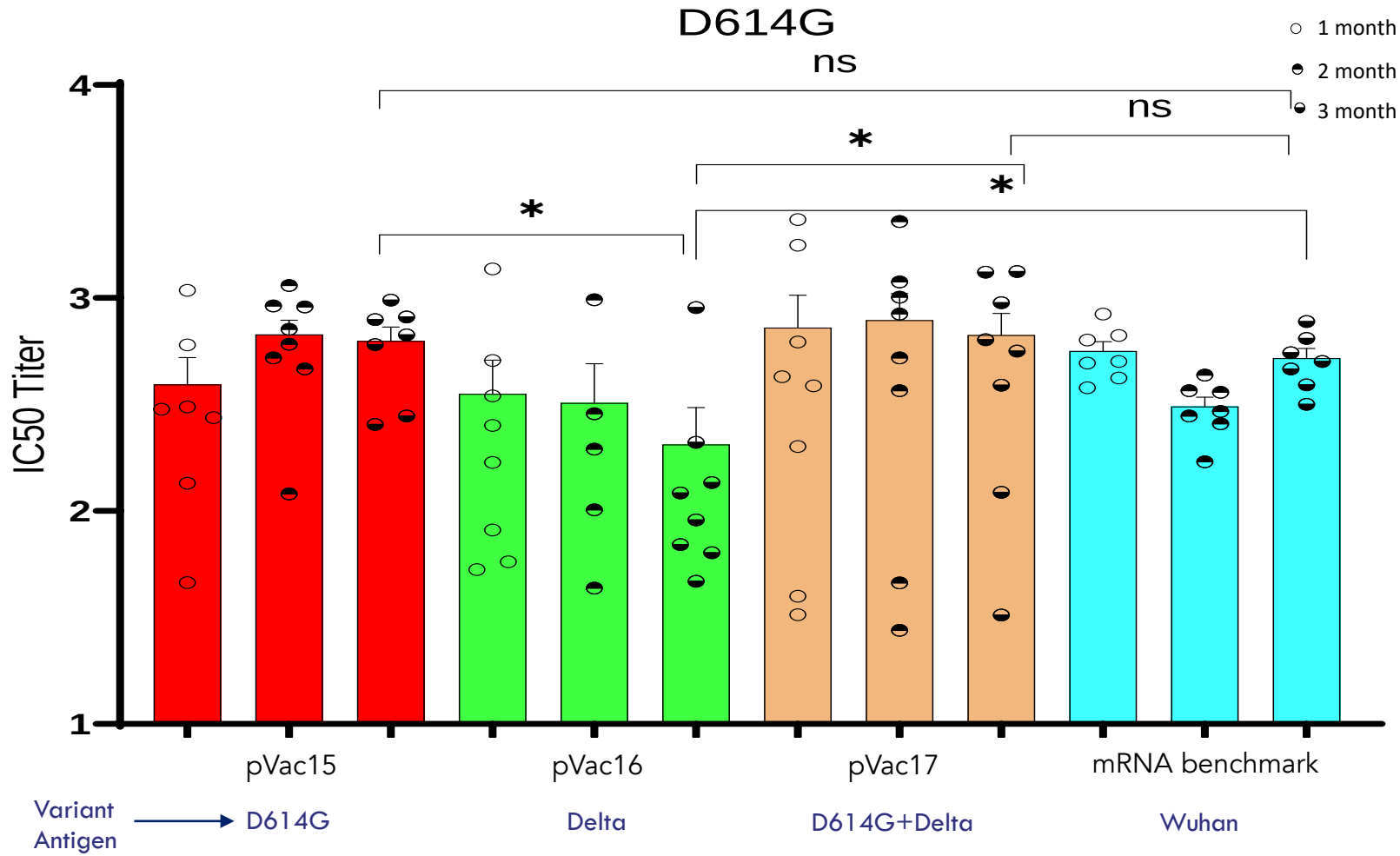
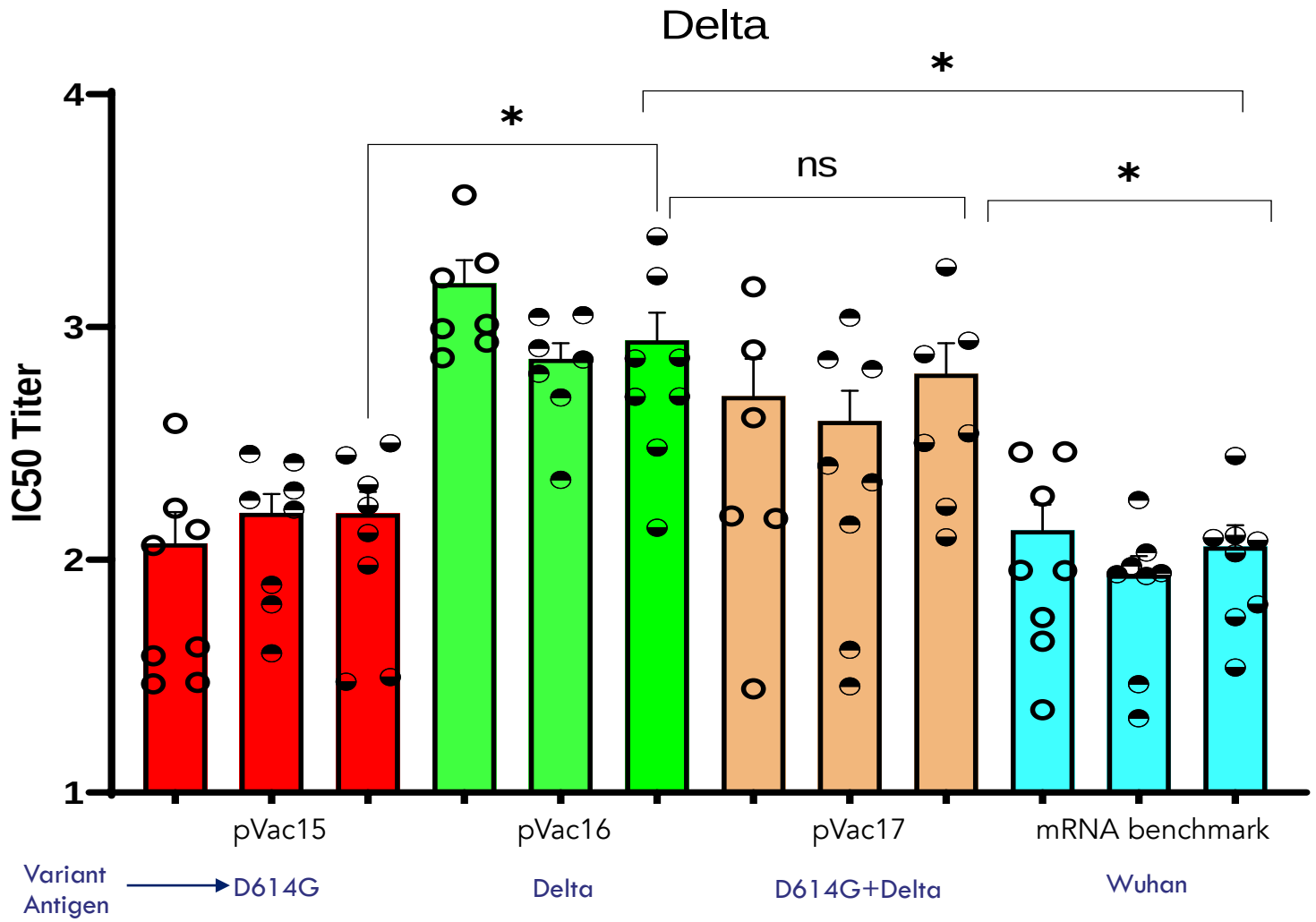
DNA Vaccine Produces A Long-Term Functional Response (D614G variant)

Persistence of Neutralizing Response at 3 months After Boost



DNA Vaccine Produces A Long-Term Functional Response (Delta variant)

Persistence of Neutralizing Response at 3 months After Boost

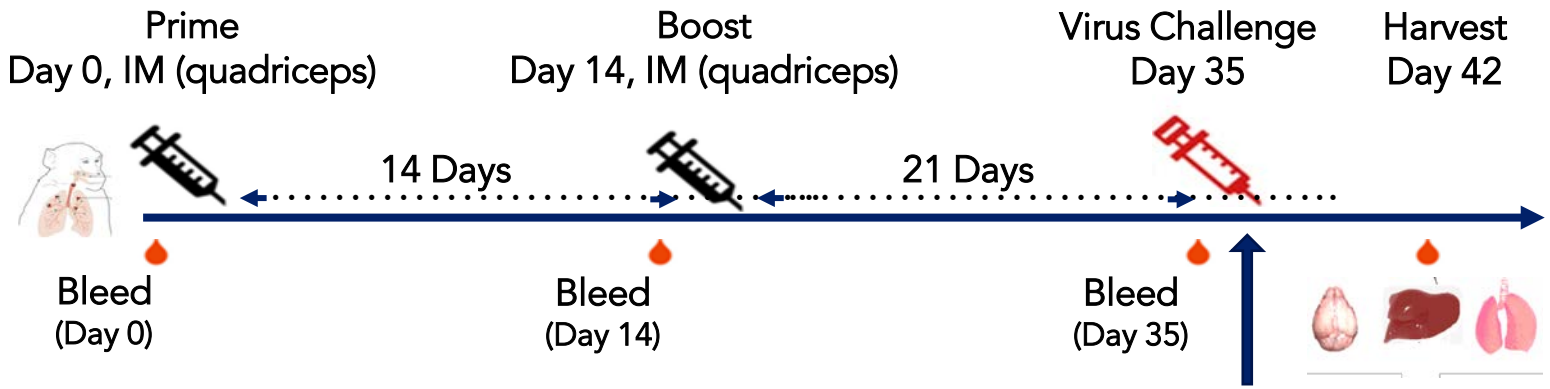


Mouse Challenge Study (April 2022 start)

- Vector: pVac-15 (D614G), pVac-16 (Delta), pVac-17 (D614G + Delta)
- Formulation: F3

Group	hACE2	vaccine	variant	DNA dose	volume
1	10*	placebo	-	-	100µl
2	5	pVac-15	D614G	125µg	100µl
3	5	pVac-16	Delta	125µg	100µl
4	10*	pVac-17	D614G/Delta	125µg	100µl

* Five animals for each variant challenge

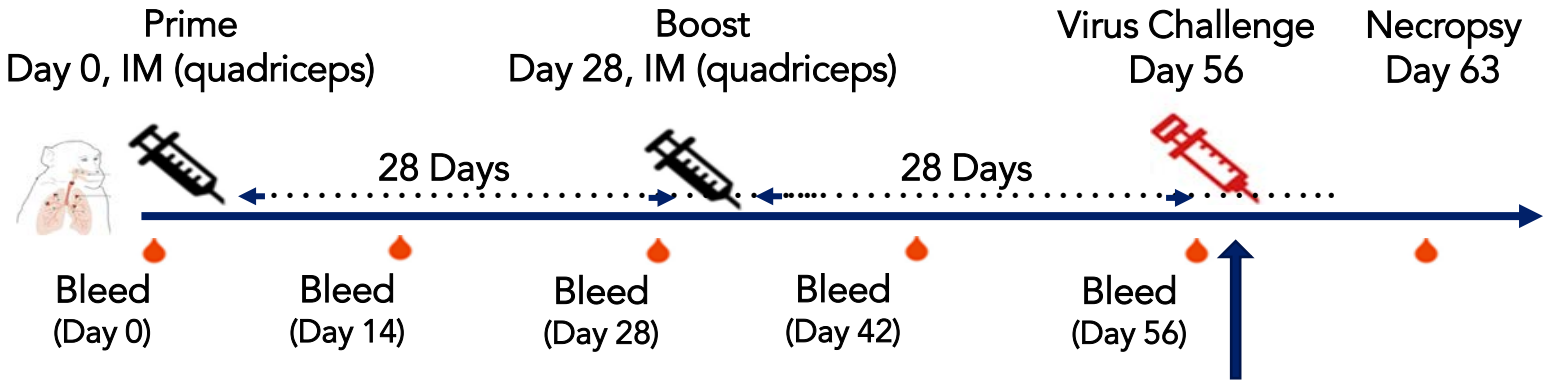


NHP Challenge Study (April 2022 start)

- PLACCINE Vector pVac-15 (D614G)
- Formulation: F3
- 28 cynomolgus (Age 3-6 years)

Group	NHP	vaccine	# doses	dose	variant	volume
1	6	placebo	2	-	-	1ml
2	6	mRNA comparator	2	100 ug	D614	500µl
3	6	pVac 15	2	1.0 mg	D614G	1ml
4	6	pVac15	2	5mg	D614G	1ml
5*	4	pVac15	2	5mg	D614G	1ml

* ≥6-month durability followed by challenge



Summary & Current Studies

Summary

- Evidence of immunogenicity against SARS-CoV-2 antigen
  - IgG, nAb, and T-cell responses
- Activity demonstrated with both single & bi-cistronic vectors
- Immune quality is comparable to commercial mRNA vaccine benchmark

Current Studies

- Immune response durability
- Dose response, safety toxicity, and biodistribution
- Challenge studies – rodent and NHP
- Ongoing Stability studies at optimal commercial conditions

Broad Vaccine Pipeline Opportunity Following Proof of Concept

Initial POC/Validation Target

Potential Pathogen Targets

Future Pipeline Criteria

- Unmet need
- Conventional approaches ineffective
- Suitable for DNA approach

Immediate Next Candidates

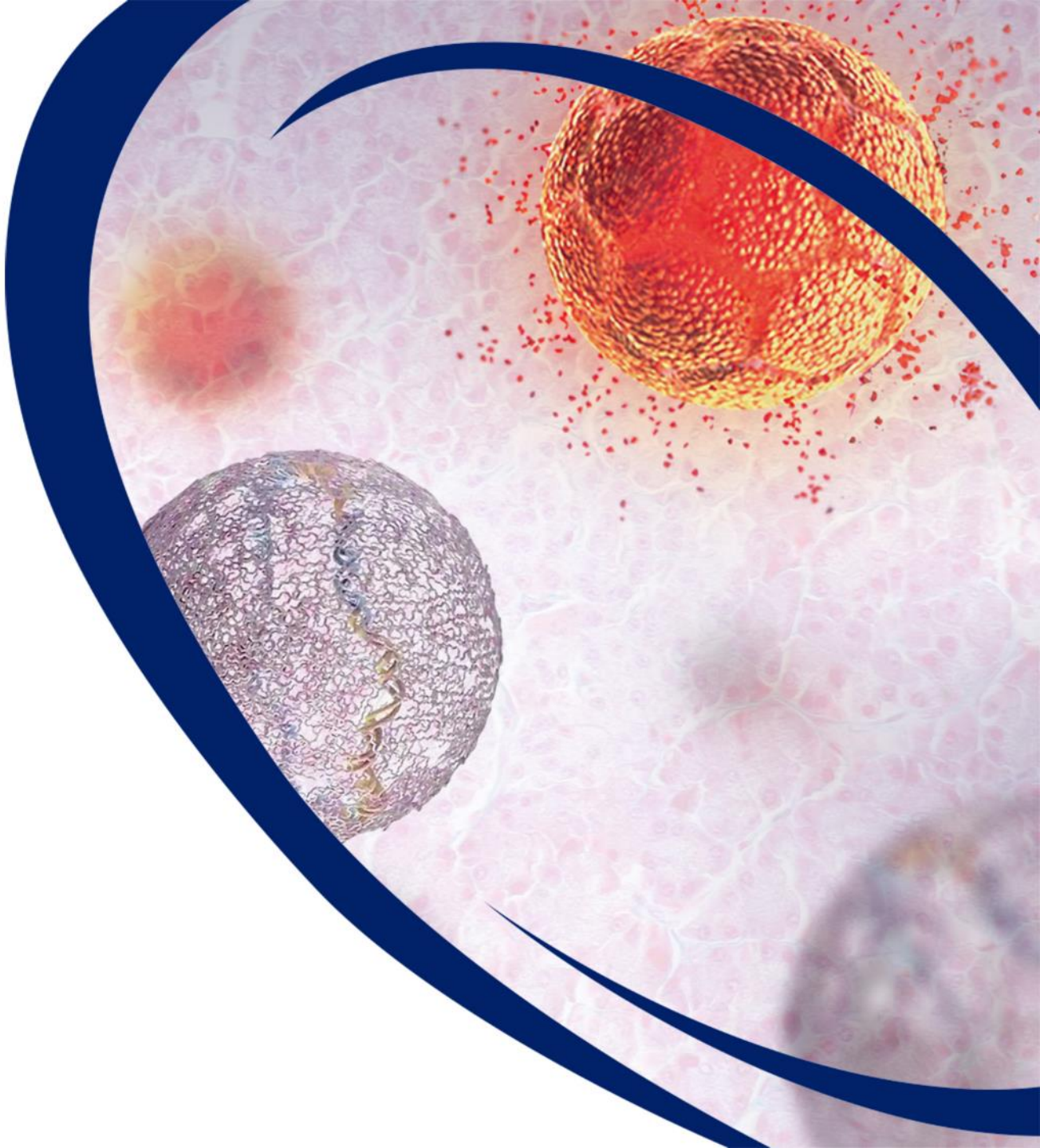
- CMV
- RSV
- Influenza

Applicable to Cancer Targets

- Melanoma (Trp2, gp100)
- Ovarian cancer (NY-ESO1, mucin1)

Financials

Management Team



Financial Overview

Cash + Investments at 3/31/2022	$47.3 million
April 2022 Equity Offer (At-the-Market)	+ $6.5 million
Projected NOL sales – 2022-2024	+ $3.5 million
Total	**$57.3 million**
Estimated cash usage/quarter (2022)	$4.75 million
Cash Runway at current spending	1st Half of 2025

Common shares outstanding at 5/15/2022	7.1 million
+ Stock Options	0.7 million
+ Warrants	0.2 million
Fully diluted shares outstanding	**8.0 million**
Market Capitalization	**$25 million**
Avg Daily Trading Volume	~ 300,000

Celsion

Celsion

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