CaroGen Corporation

Creating a Wave of Transformative Immunotherapies...

Developing Novel Immunotherapies For Solid Tumors and Infectious Diseases

Bijan Almassian, PhD
CEO

AVIDIO Platform & Pipeline

Platform: ***AVIDIO*** (***A***rtificial ***V***irus for ***I***nfectious ***D***iseases and ***I***mmuno-***O***ncology) with worldwide exclusive rights from Yale

Oncology: CARG-2020, an oncolytic virus

Ovarian Cancer & Solid Tumors

Infectious Disease: CARG-301

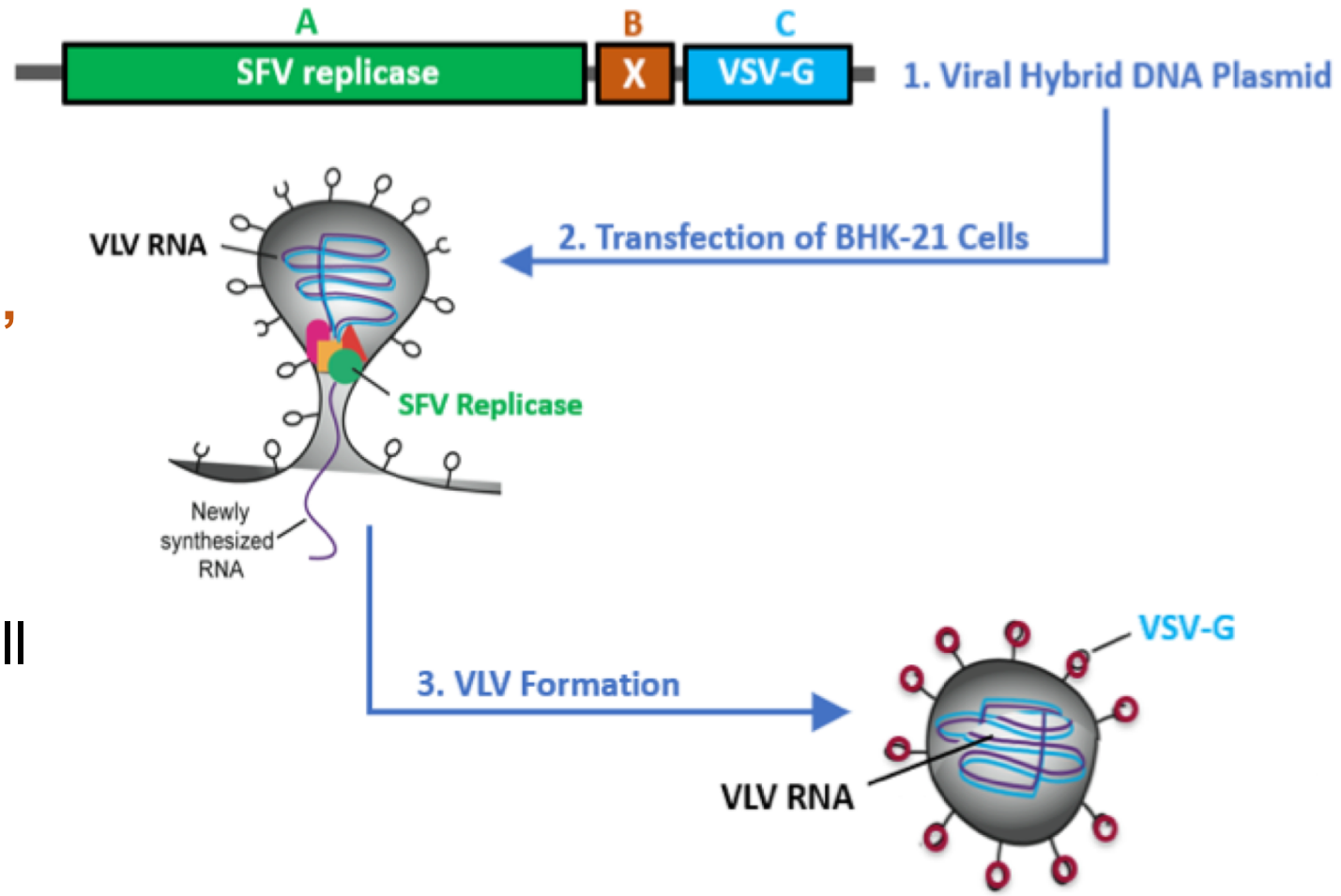
Functional cure for chronic HBV infected patients. Funded by NIH ($5 Million)

AVIDIO Comprised of Two Viruses and Possess High Payload Capacity

A: Semliki Forest Virus (SFV) facilitates gene expression

B: **Payload (X: antigens, cytokines, shRNA or combination)**

C: **Vesicular Stomatitis Virus Glycoprotein (VSV-G)** facilitates cell entry



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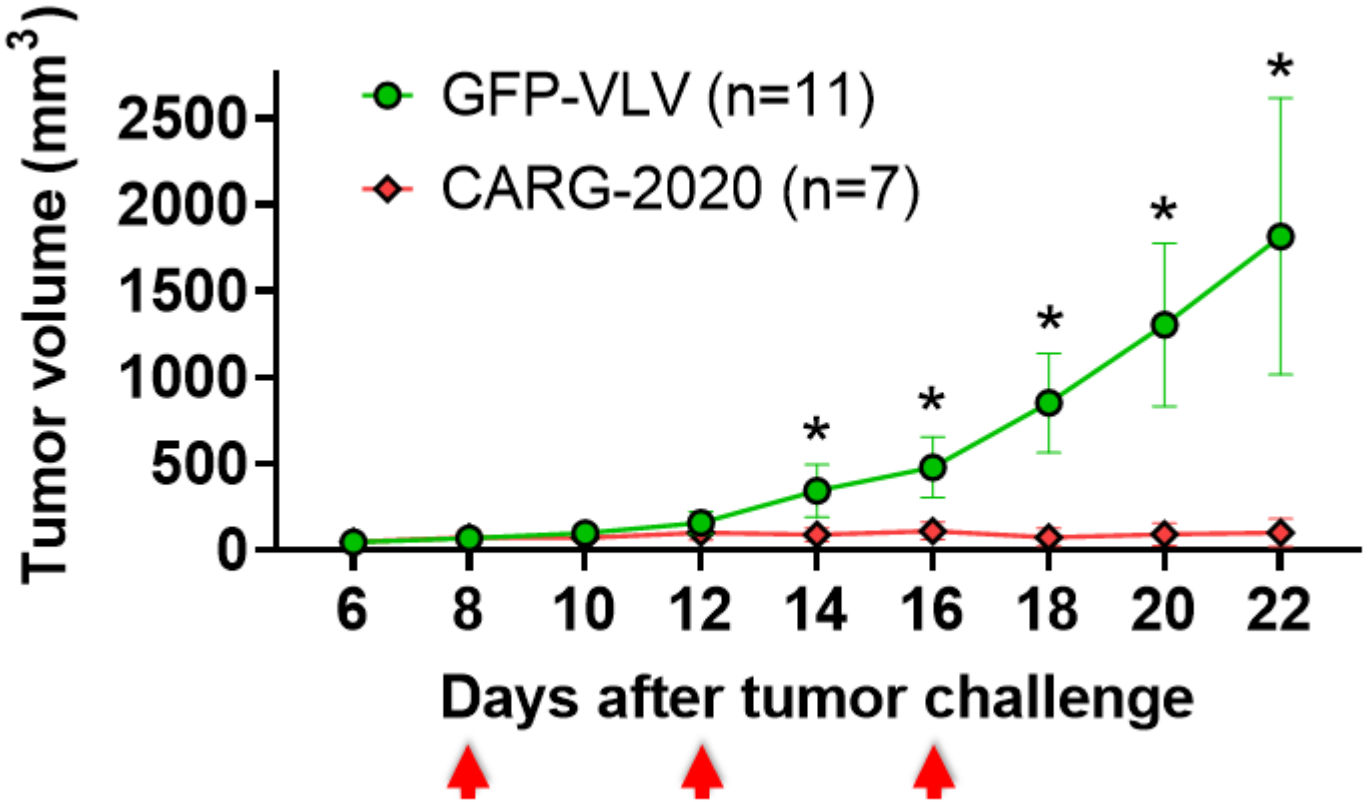
Source: Rose *et al*. PNAS (2014) **111**:16866-71

CARG-2020: Oncolytic Platform Designed to Target Multiple Pathways

Rationale:

IL-12	**Amplify** anti-cancer immune response
IL-17RA antagonist	**Expand** immune response by blocking tumor-promoting inflammation
shRNA-PD-L1	**Sustain** anti-cancer immunity by blocking immune checkpoint pathway

CARG-2020 Intravenously Inhibits Tumor Growth Significantly in Syngeneic Mouse MC38 Colon Cancer Model



Days of injection

Injection dose: 1 x 10^8 PFU per mouse per dose, IV

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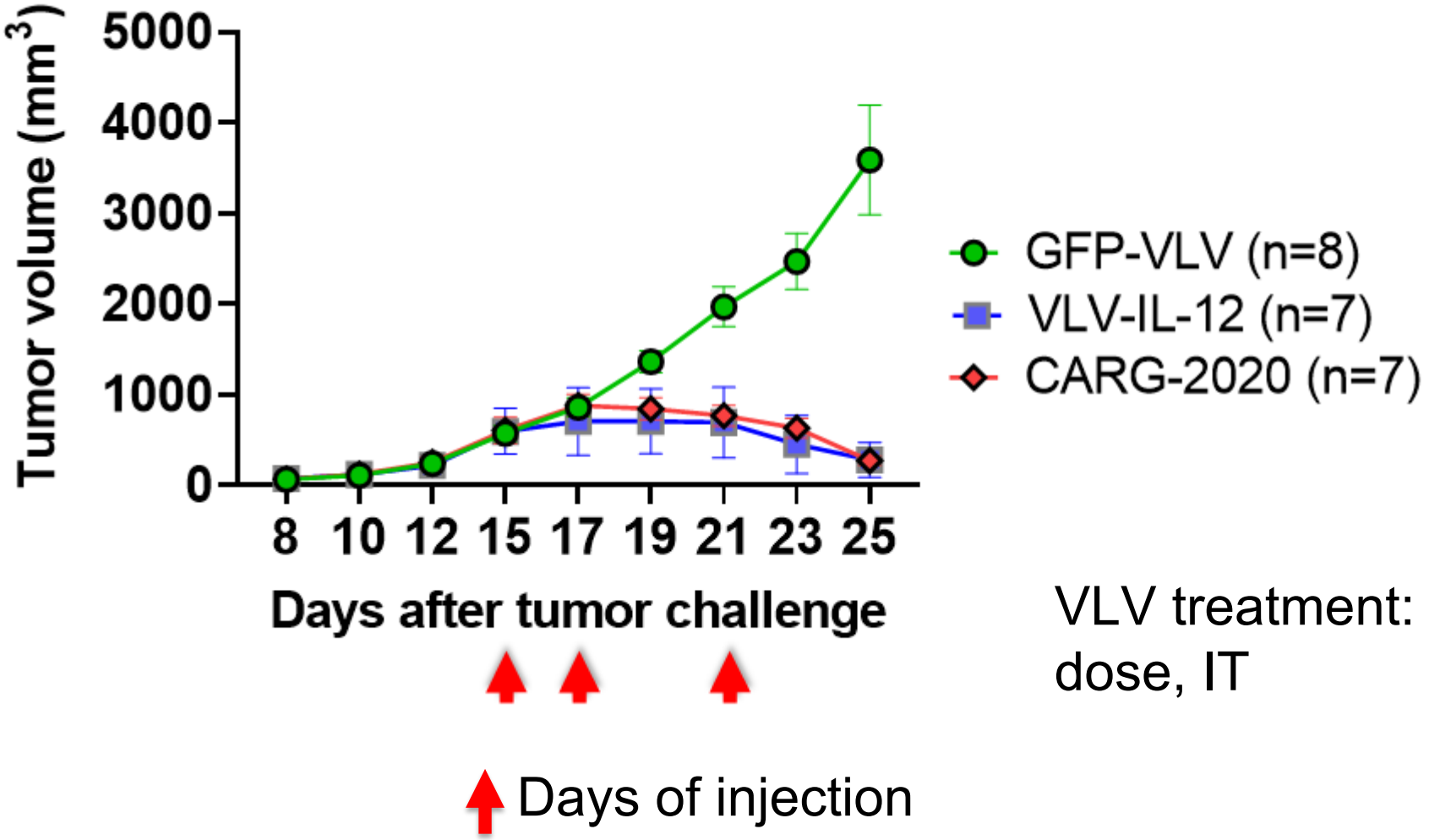
CARG-2020 Intratumorally Reduces Tumor Growth Significantly in MC38 Colon Cancer Model



VLV treatment: $5x10^7$ PFU per dose, IT

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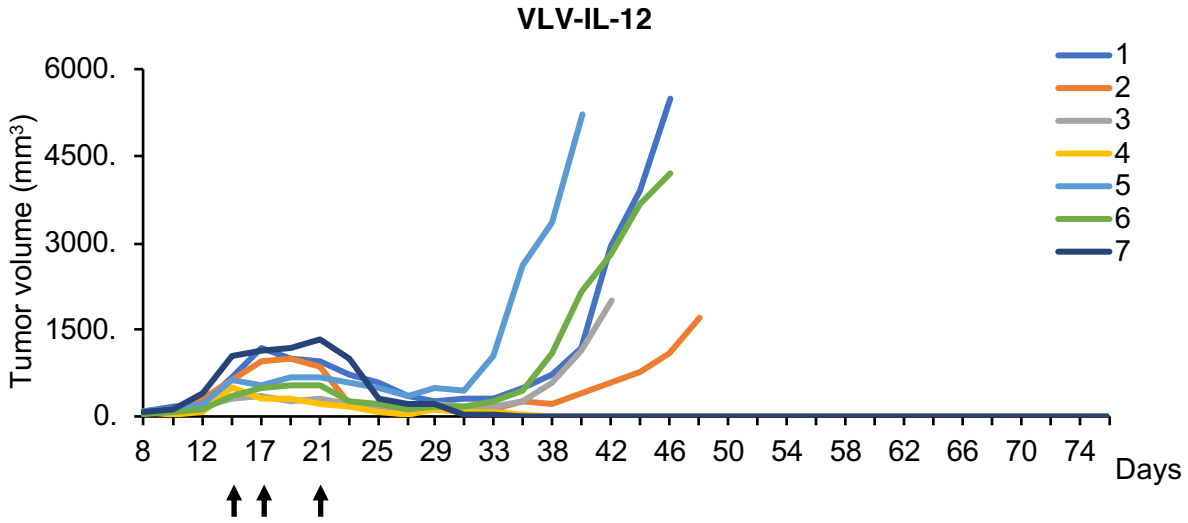
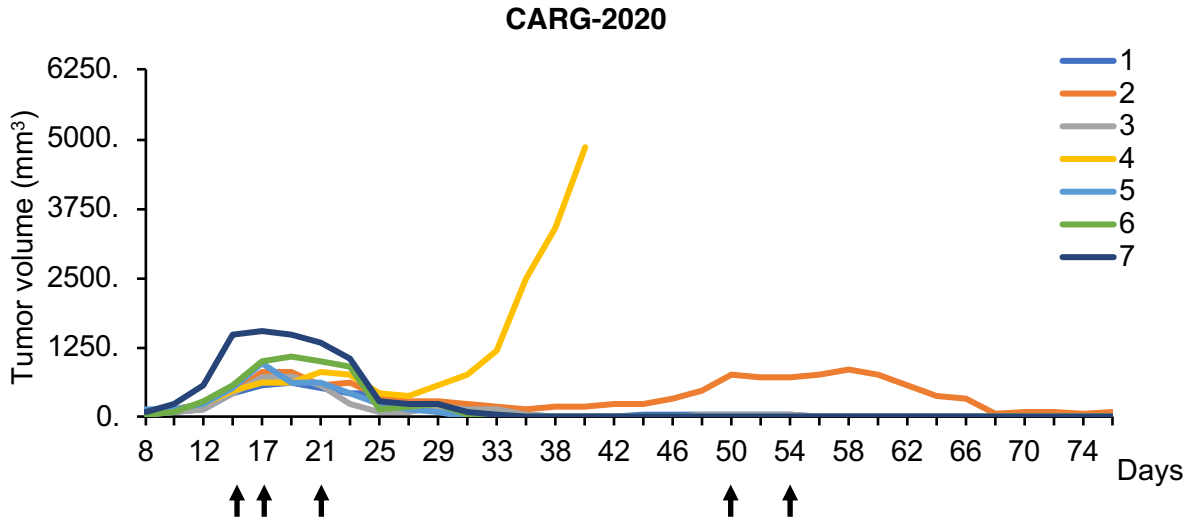
CARG-2020 IT, SUPERIOR TO VLV IL-12 IN PREVENTING TUMOR RECURRENCE

CARG-2020 achieved complete tumor elimination in 6 out of 7 mice.





Arrows indicate days of injection.

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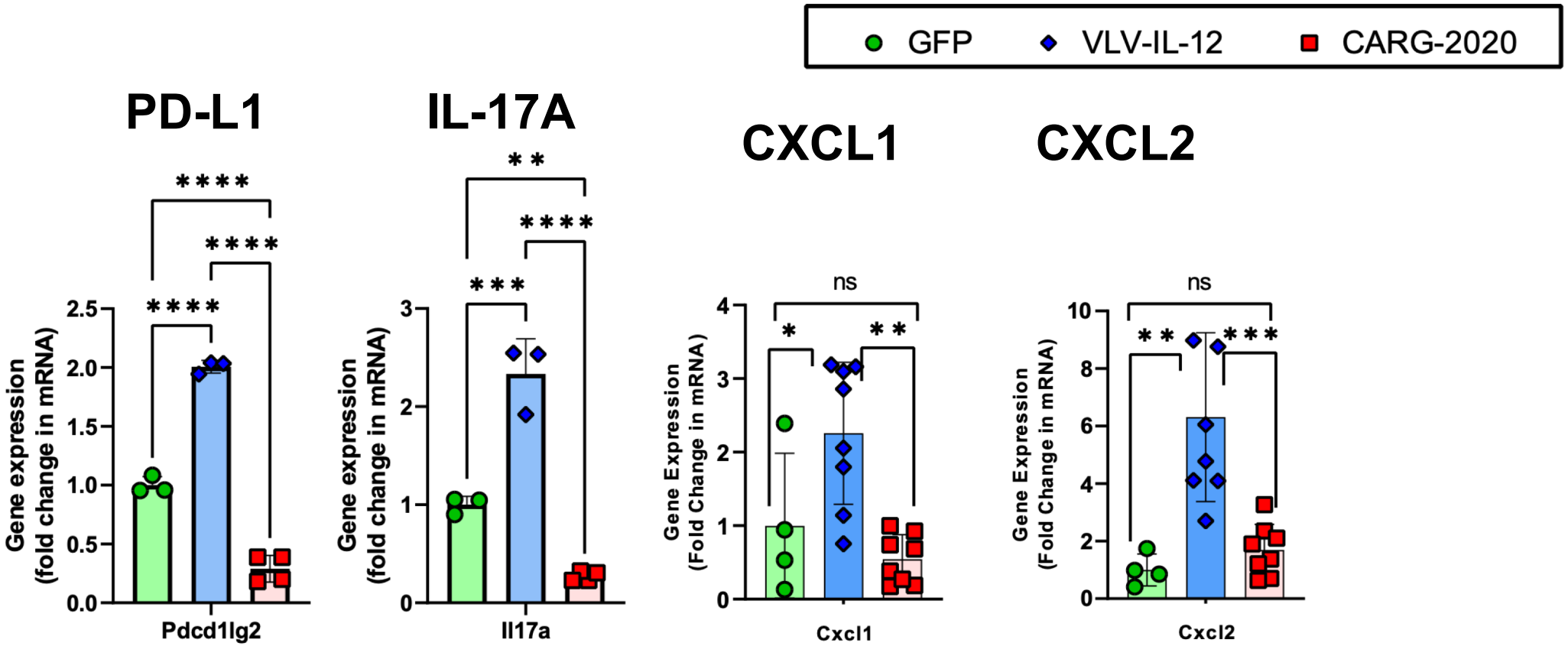
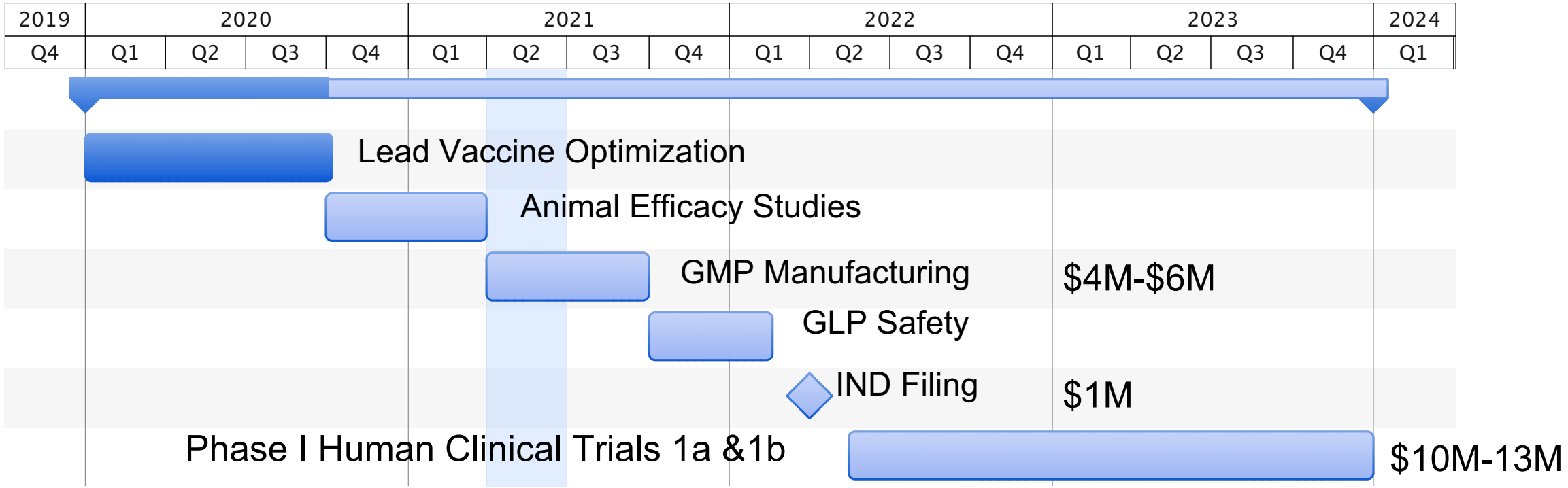
CARG-2020 Inhibits Expression of Immune Checkpoint, IL-17 and IL-17-induced Chemokines



Development of CARG-2020 for Ovarian Cancer



Pre-IND meeting with the FDA is planned for Summer 2021

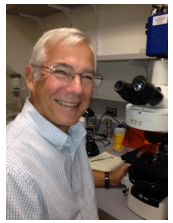
EXECUTIVE TEAM AND SCIENTIFIC ADVISORS

Bijan Almassian, PhD;
Co-Founder, President & CEO, Board of Director
Vion, Panacea, Genzyme, Genelabs

Valerian Nakaar, PhD;
Co-Founder, CSO, Sr. Vice President, Board of Director
VaxInnate, Vion, Yale University Sch. Med.

Gil G. Mor, MD, PhD; SAB
Professor and Scientific Director , C.S, Mott Center, Wayne State University School of Medicine, Professor Yale School of Medicine

Kepeng Wang, PhD; SAB
Assistant Professor at UConn Health
University of Connecticut



John Rose, Ph.D.,
Co-Founder and Chairman SAB
Professor, Pathology, and Director, Program in Virology and Vaccine Development ,Yale University School of Medicine

Michael Robek, Ph.D.,
Co-Founder, Member of SAB
Professor, Albany Medical College and former Associate Professor at the Yale University School of Medicine

Jack R. Wands, MD; SAB
Professor and Director, Liver Research Center, Brown University School of Medicine

Steven Geary, PhD; SAB
Professor Pathology and Veterinary Science Department of Molecular and Cell Biology, University of Connecticut

CaroGen Highlights

- Novel platform technology with broad application
- Portfolio: Two clinical candidates
  - CARG-2020 for cancer
  - CARG-301 for HBV
- Issued patents
- Seeking $25 million: Filing two INDs within 18 months, IPO within 24 months
- Experienced Management Team, SAB, BOD

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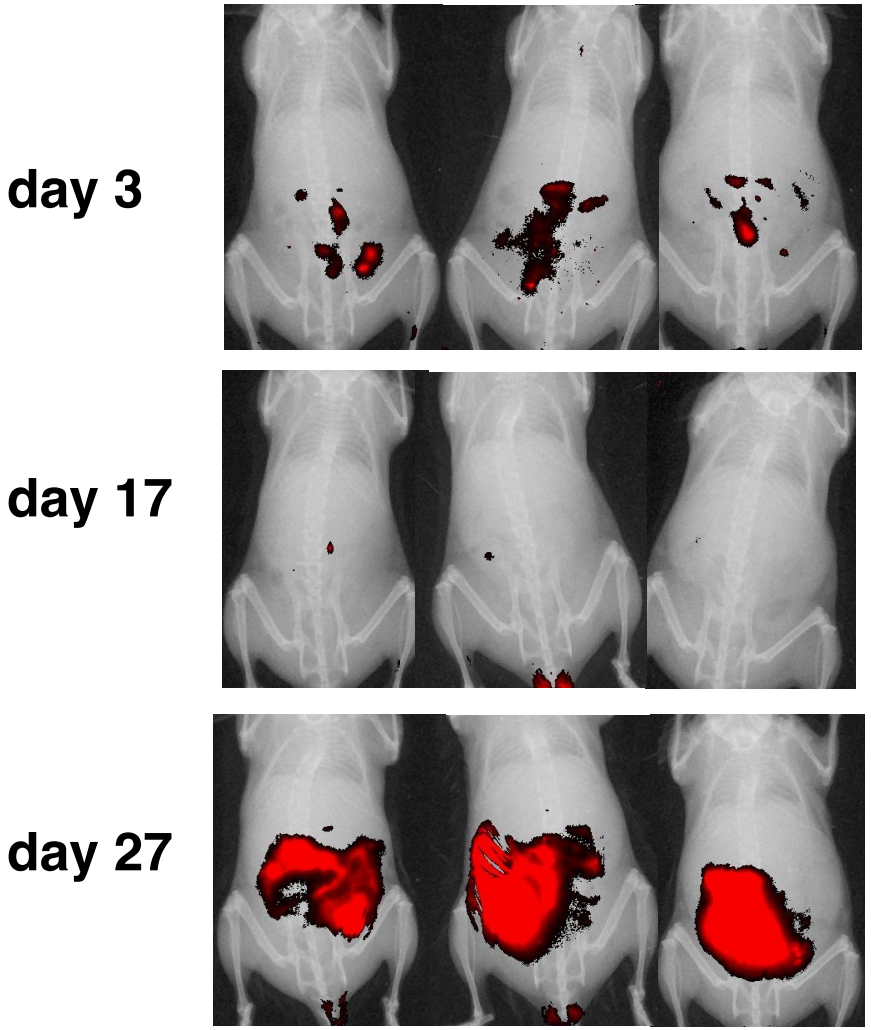
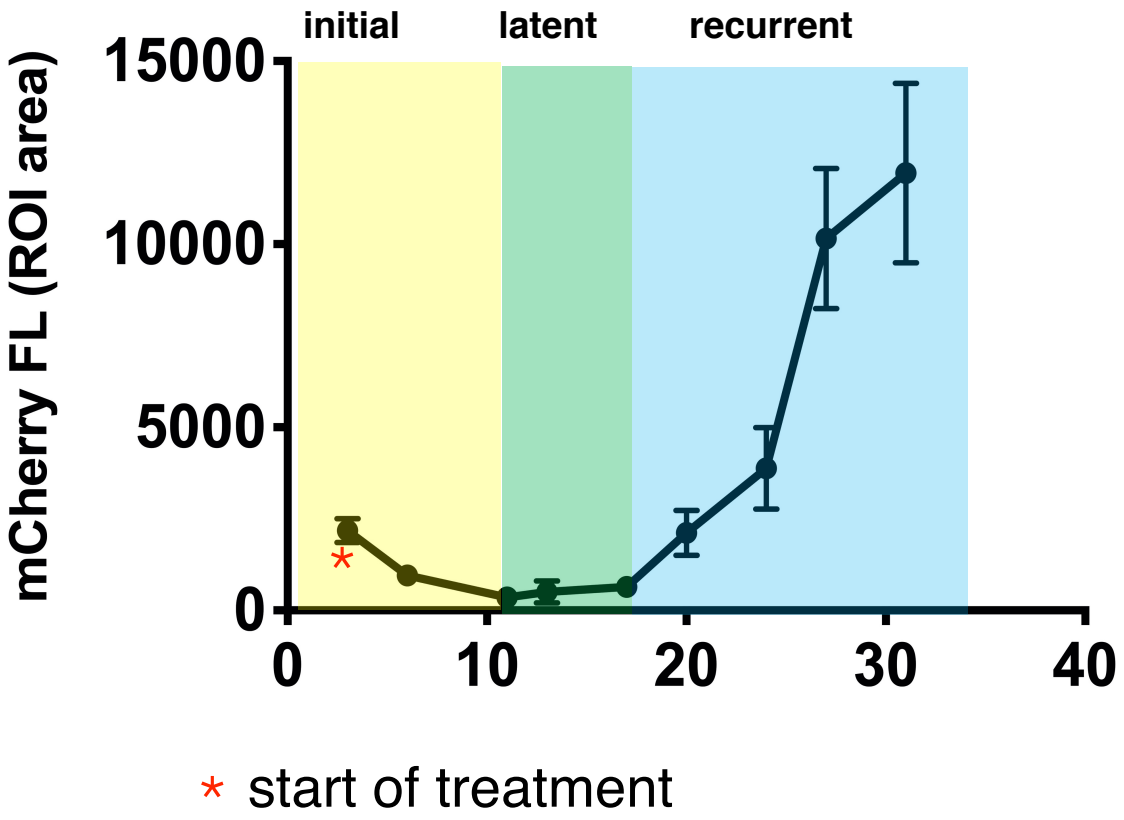
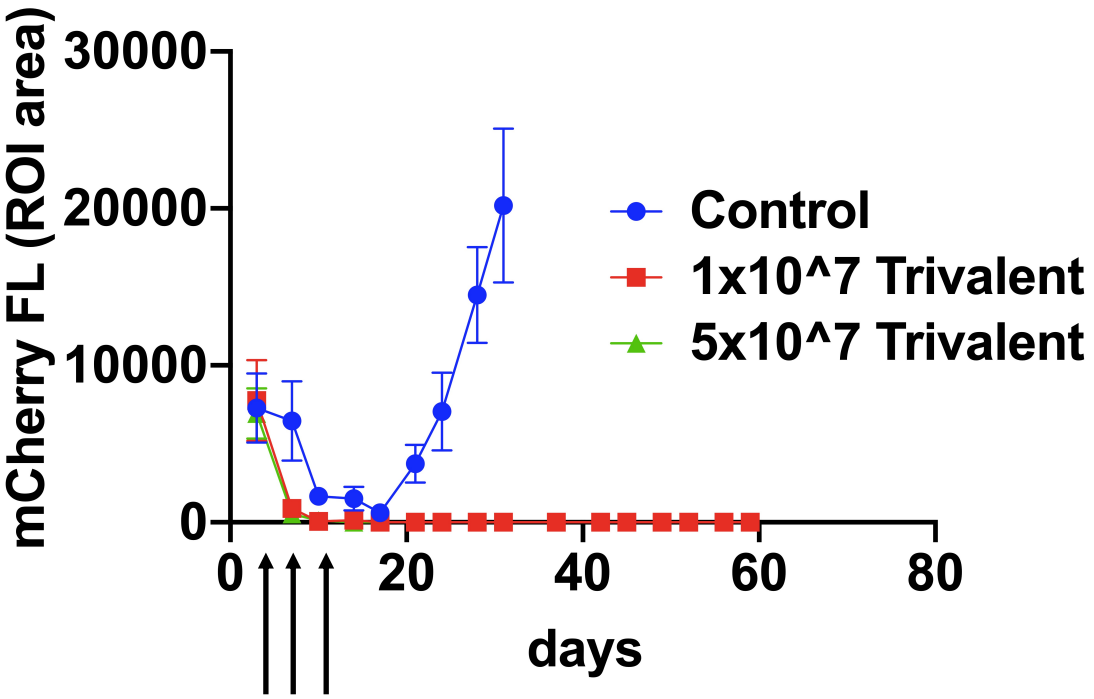
OVARIAN CANCER TKO IMMUNOCOMPETENT CARCINOMATOSIS MOUSE MODEL WITH CHEMORESISTANT OVARIAN CANCER CELLS

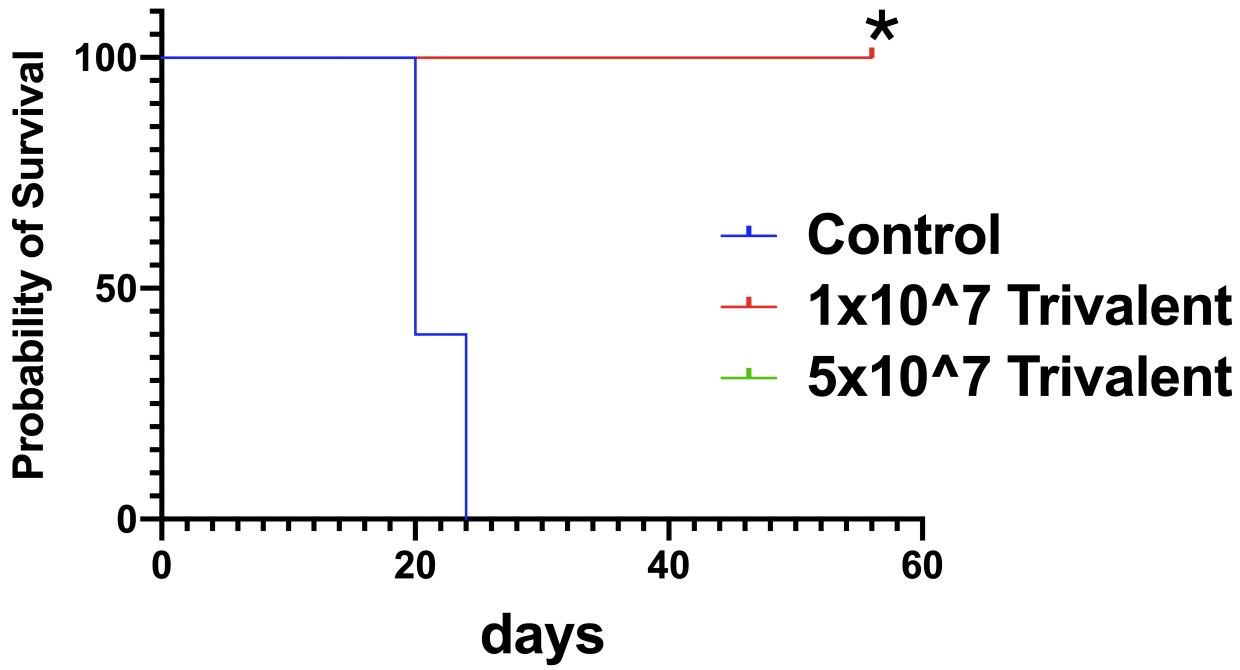




Alvero et al., 2020, Oncoimmunology, 9:1758869

CARG-2020 (TRIVALENT) BLOCKS TUMOR RECURRENCE AND EXTENDS OVERALL SURVIVAL





Injection Days 3, 5 and 7
Control: PBS

* p = 0.0011

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AVIDIO

Development of CARG-301 for Patients Chronically Infected with Hepatitis B Virus (HBV) Infection

MICHAEL ROBEK, PH.D.
PROFESSOR
ALBANY MEDICAL COLLEGE
MEMBER, CAROGEN SAB

JOHN ROSE, PH.D.
PROFESSOR
YALE U SCH OF MEDICINE
CHAIR, CAROGEN SAB

CARG-301: A CLINICAL CANDIDATE FOR FUNCTIONAL CURE OF HBV PATIENTS

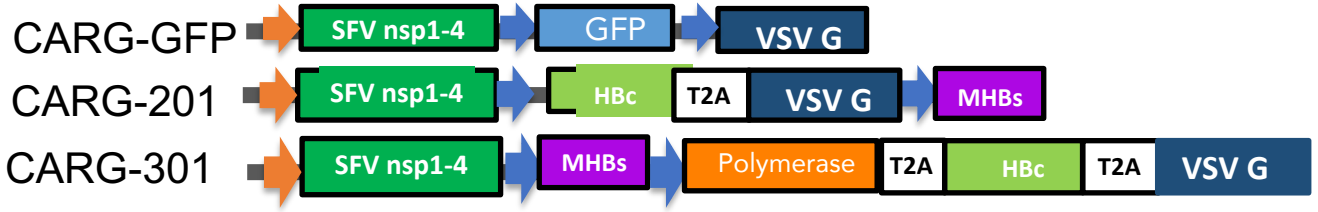
CARG-301 is delivering transgenes for three HBV antigens (MHBs, HBc and polymerase):

- Enables robust expression and secretion of HBV middle S, core and polymerase antigens *in vitro*
- Reduces surface antigens by more than 2 logs in AAV model
- Preclinical development is fully funded by NIH ($5M)

VLV Platform and HBV Publications:

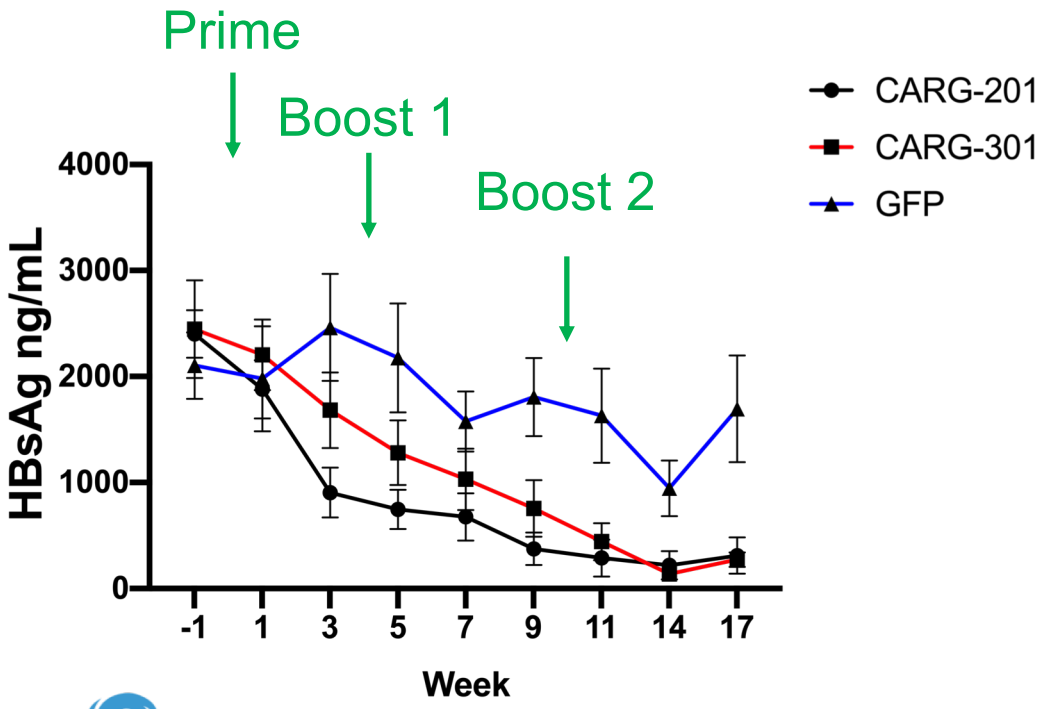
Rose et al. *PNAS* (2014) 111:16866
Reynolds et al. *J Virol* (2015) 89:10407
Van den Pol et al. *J Virol* (2017): 91:e02154
Yarovinsky et al. *iScience* (2019) 21:391
Chiale et al. *Antiviral Res* (2019) 168:156
Chiale et al. *Vaccines* (2020) 8:279

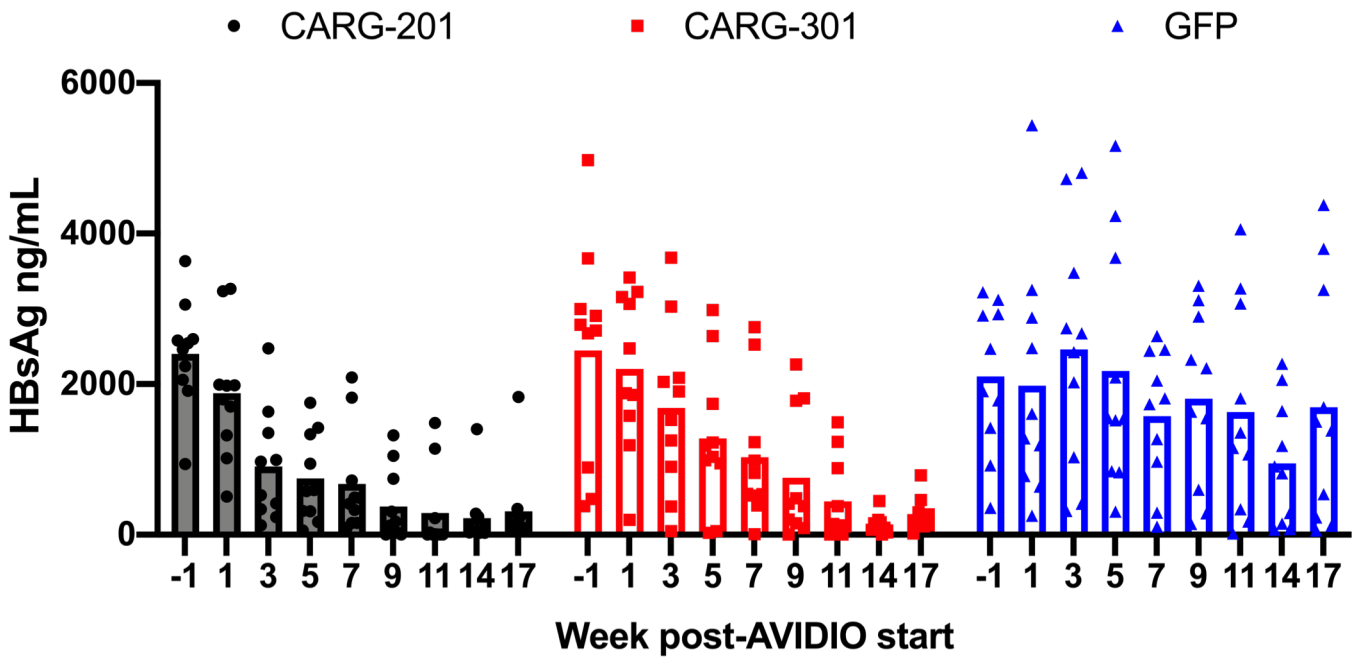
CARG-301 PRIME-BOOST SIGNIFICANTLY REDUCES HBsAG IN MICE WITH HIGH HBV ANTIGEN LEVELS



2 HBV antigens

3 HBV antigens





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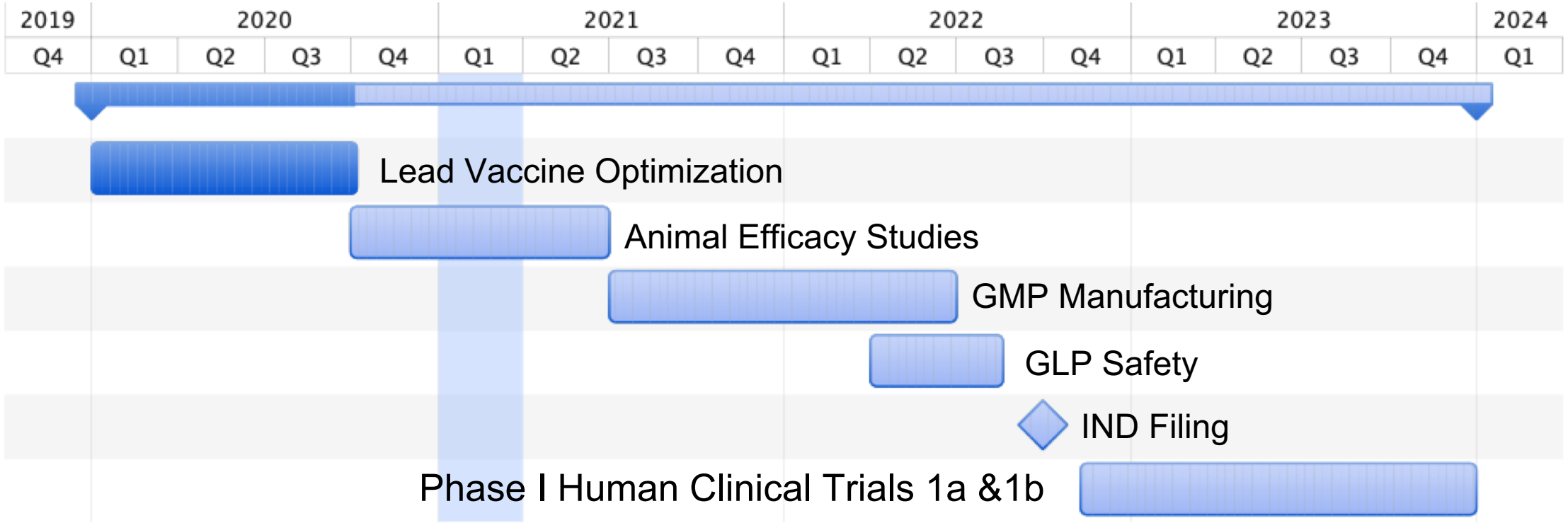
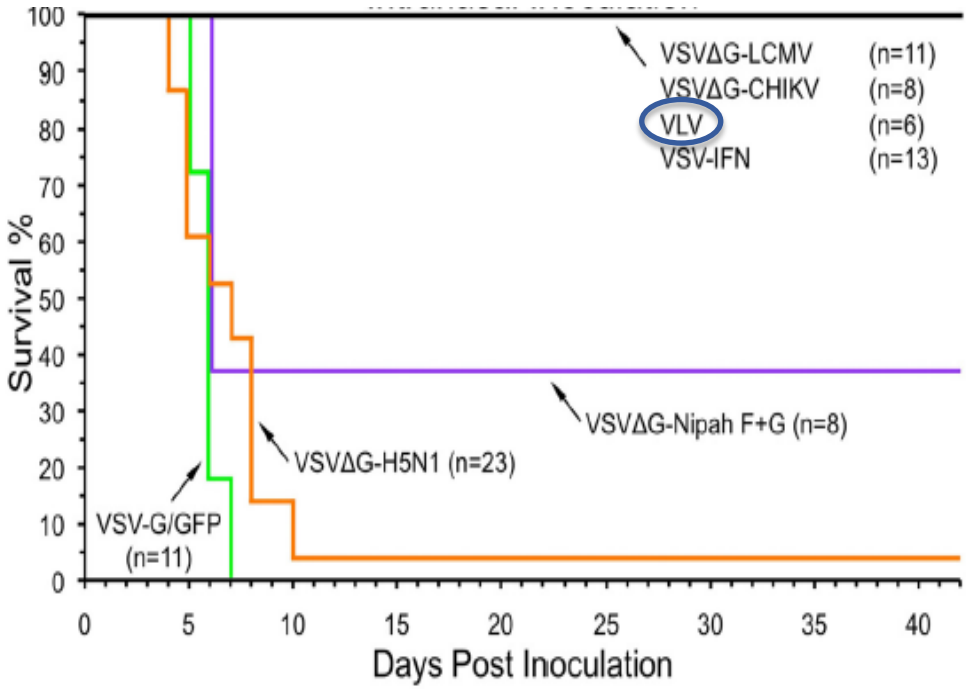
CARG-301(HBV) DEVELOPMENT PLAN: TIMELINE, BUDGET & DELIVERABLES

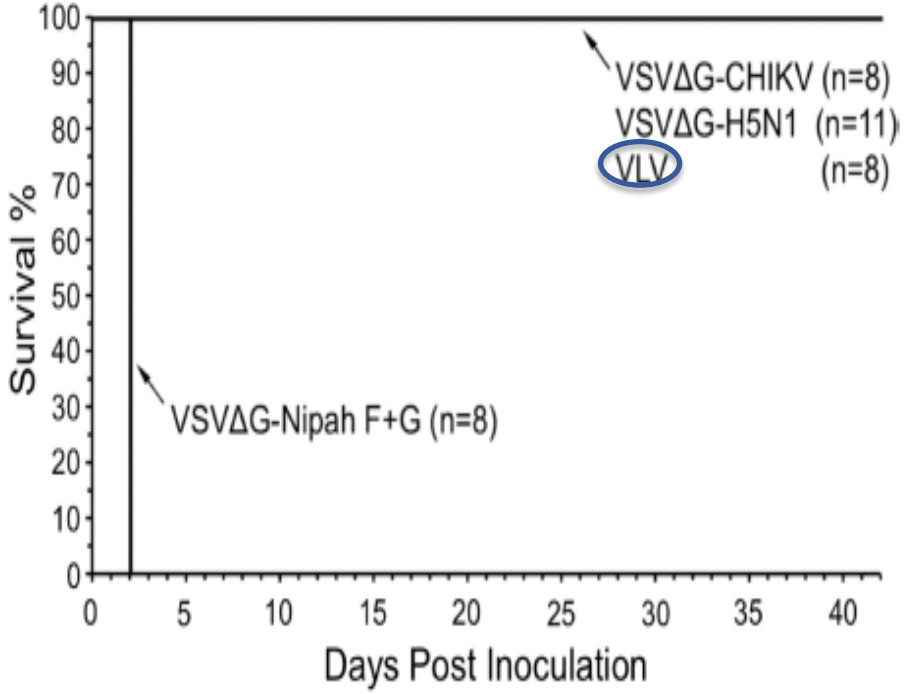


AVIDIO is Safe

Intranasal



Intracranial



100% of mice survived after VLVs were administered intranasally or intracranially

van den Pol et al (2017) *J Virol* 91:e02154

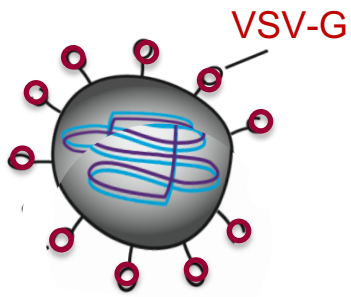
INTELLECTUAL PROPERTY

- Composition of Matter: *Evolution of High-Titer Virus-Like Vesicles for Vaccine Applications*
  - PCT/US2015/030102, filed 5/11/2015
    - National Phase, November 15, 2016
    - US, EU, China, India, Australia, Brazil, Canada, Japan
    - Issued on October 8, 2019, Patent # 10435712

- Method of Use: *Virus-Like Vesicles Based Vaccines to Prevent or Treat Chronic Hepatitis B Virus (HBV) Infection*
  - PCT/US2015/030100, filed 5/11/2015
    - National Phase, November 15, 2016
    - US, EU, China, India, Australia, Brazil, Canada, Japan
    - Issued on 6/5/2018:U.S. Patent No. 9,987.353

- Composition and Methods of Use of Oncolytic Virus Like Vesicles
  - Filed on January 8, 2021
  - International Application Number : PCT/US21/12834

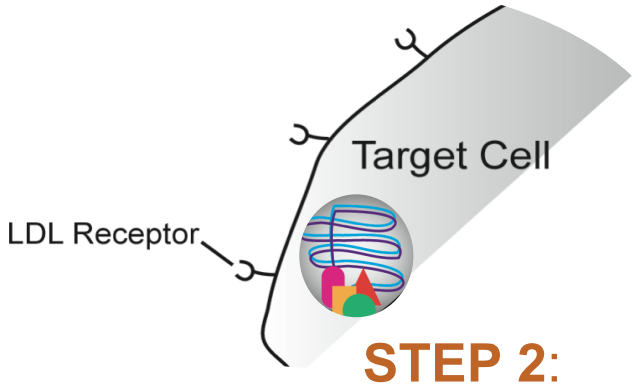
AVIDIO ENTERS TARGET CELL, EXPRESSES DESIRED PROTEINS AND INDUCES ANTITUMOR RESPONSE



VLV or AVIDIO

STEP 1:
VLV infects a target cell

Infection



STEP 2:
VLV RNA enters target cell and produces **X**

Expression

Protein X or RNAs

STEP 3:
Promotes broad immunotherapeutic effects

Induction

Antitumor and Antiviral Responses

Intra-tumoral Injection of CARG-2020 Demonstrates Abscopal Effects on Distant Un-injected Tumors

Day 0
Injection
500,000
MC38 cells

Day 6
Injection
secondary
tumor

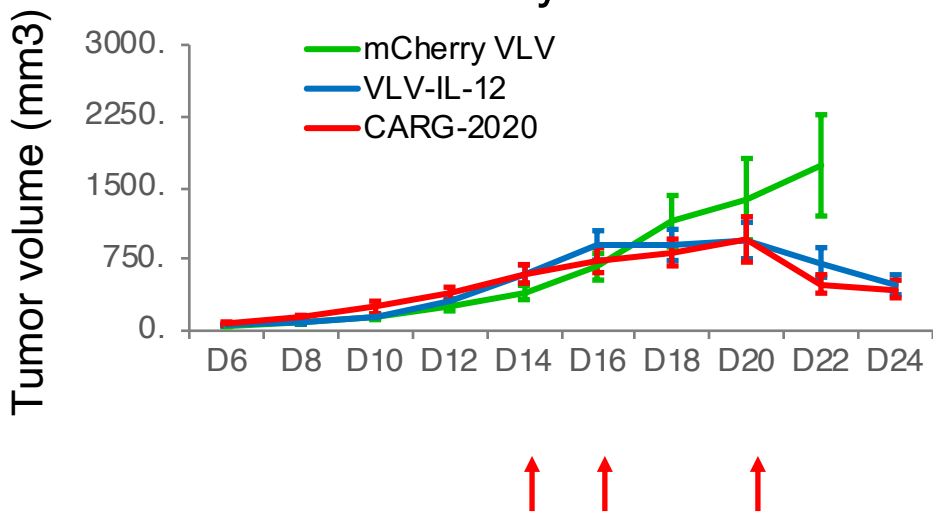
Day 14
Injection
5 x 10^7
product

Day 16
Injection
5 x 10^7
product

Day 20
Injection
5 x 10^7
product

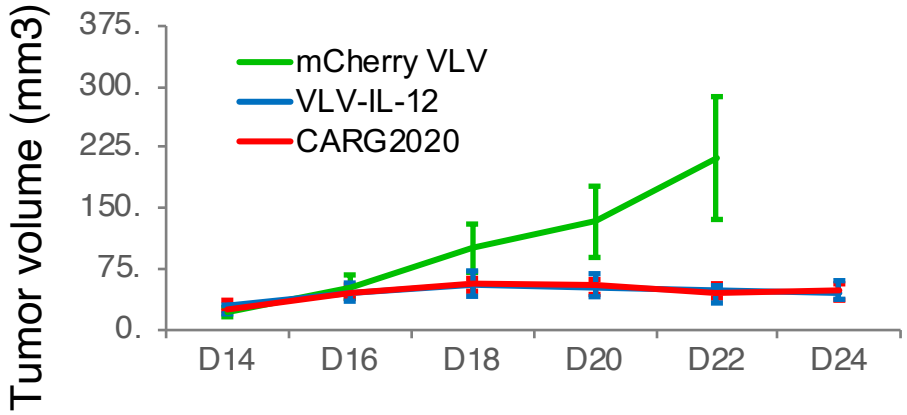
Day 24
Analysis

Primary tumor



Arrows indicate days of treatment

Secondary tumor on contralateral flank

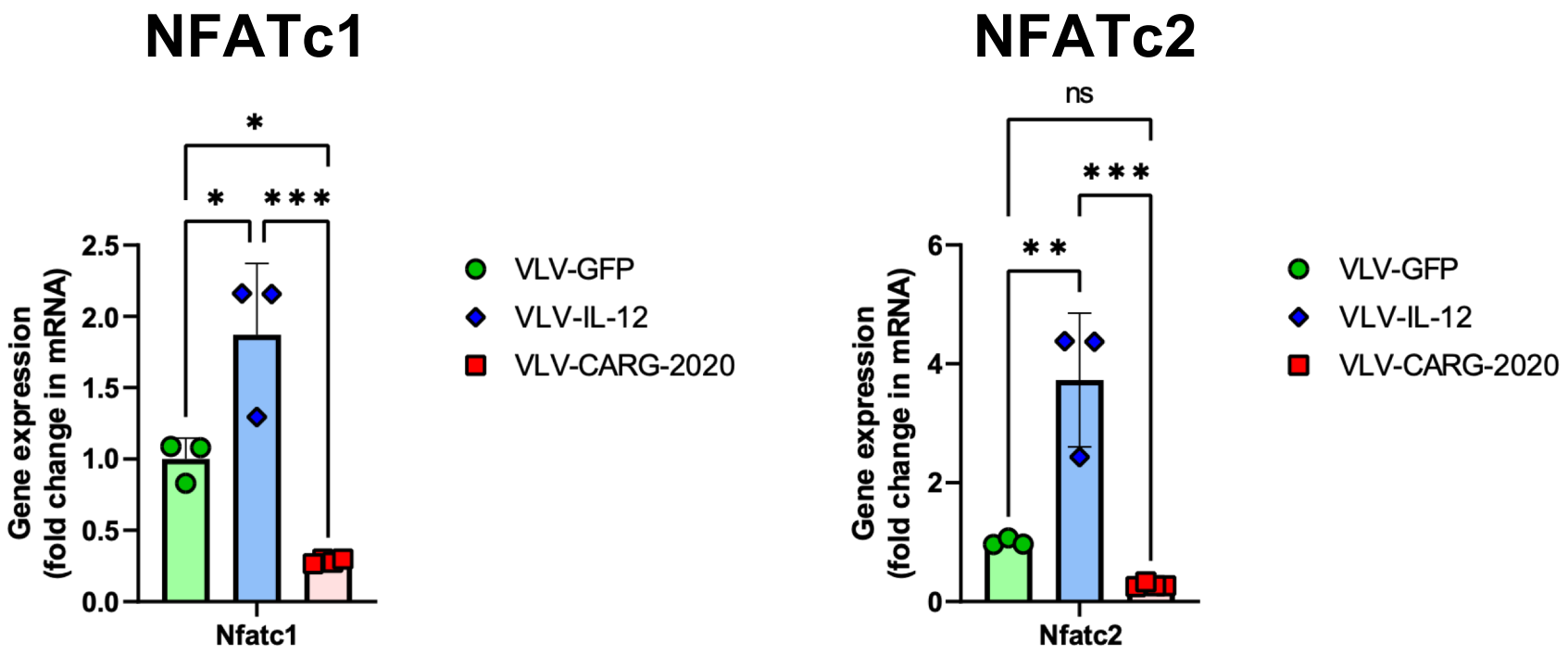


No injection treatment

Injection on right flank of mouse

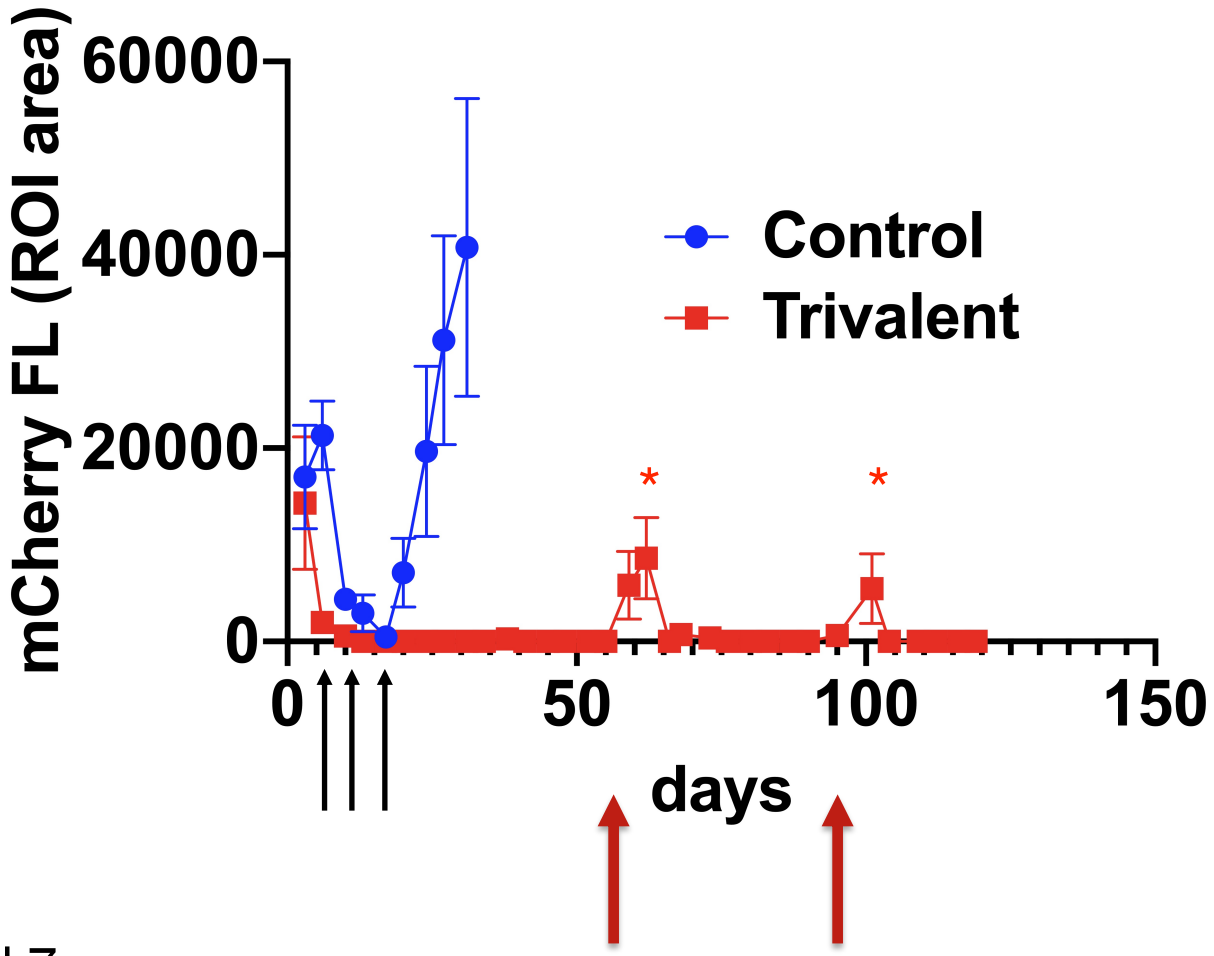
No injection on contralateral (opposite) flank

CARG-2020 IT SIGNIFICANTLY INHIBITS EXPRESSION OF NFATc1 TRANSCRIPTION FACTOR OF PRO-TUMORIGENIC ENVIRONMENT



CARG-2020 is superior to VLV-IL12 in preventing tumor recurrence

CARG-2020 PROVIDES LONG-TERM PROTECTION IN OVARIAN CANCER MODEL



Injection Days 3, 5 and 7

* re-challenged with 10^7 ovarian cancer cells

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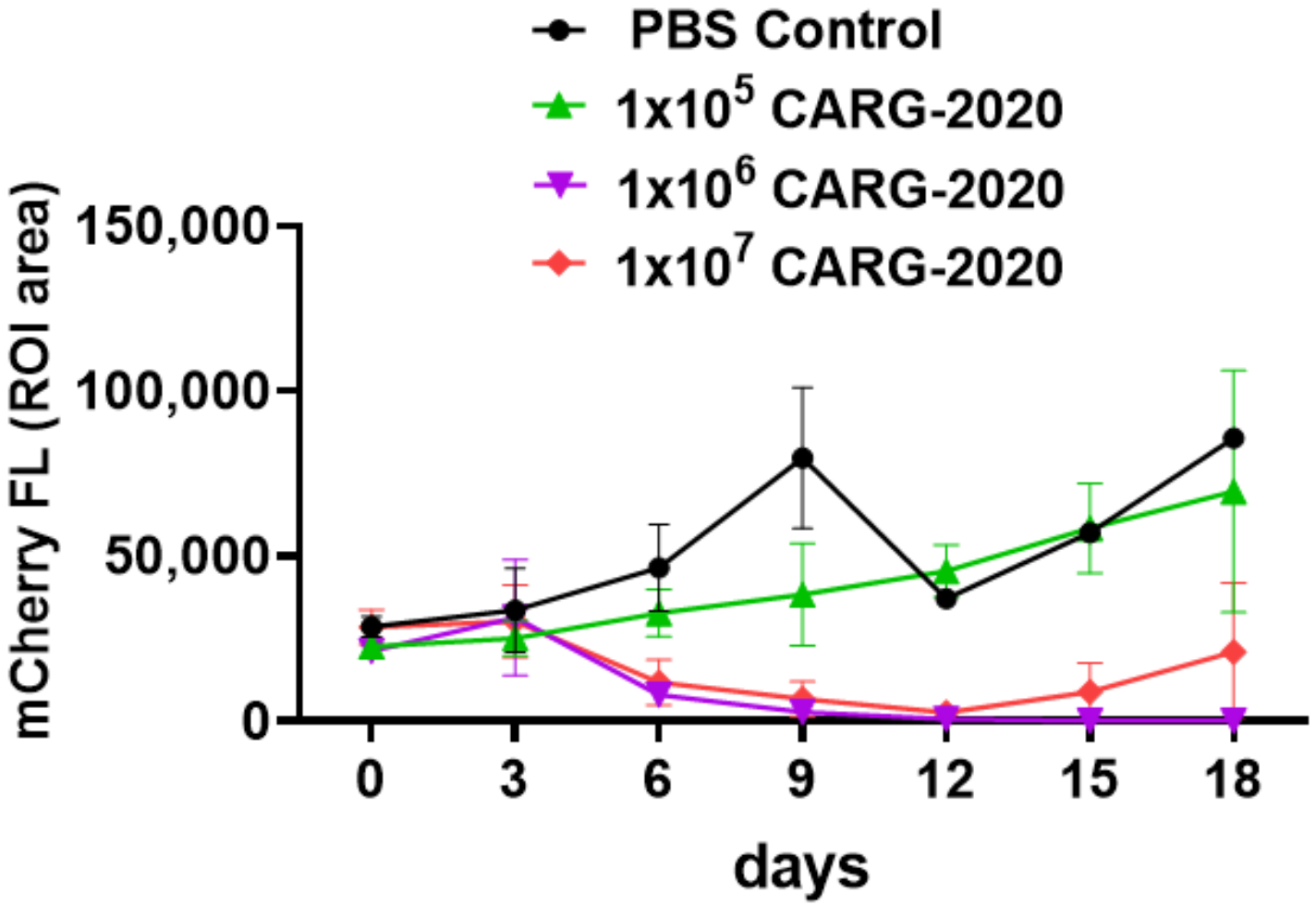
CARG-2020 Reduces Recurrence of Chemo-resistant Tumors in Dose-dependent Manner



ONCOLYTIC VIRUS FIELD COMPETITION

Company/Drug	Oncolytic Vector	Gene Target	Therapy	Stage of Development	Indication
Amgen T-Vec (Imylgic, oncovex)	HSV DNA-based	GM-CSF	Single/monotherapy	Licensed 2015	Melanoma
SillaJen Inc (S.Korea) Pexa-vec	VAV DNA-based	GM-CSF	GM-CSF---→Single Pexa-vec+chemo ---→Combo Pexa-vec +mabs ---→Combo	Ph.2 Ph.1 Ph.1	Renal cell carcinoma Melanoma, CRC, Solid tumors.
Genelux Olvi-vec	VAV DNA-based		Olvi-vec + chemo ---→Combo Olvi-vec + mabs ---→Combo	Ph.2 Ph.1	Ovarian cancer, Cervical, Various cancers
TILT Bio (Finland) TILT	Adenovirus DNA-based	TNFα + IL-12 or CD40L	TILT + α-PD-L1 mab--→ Combo TILT + α-PD-1 mab --→ Combo	IND ---→ Ph.1	Ovarian, Solid tumors
PsiOxus (U.K.) NG-641	Adenovirus DNA-based	FAP-Tac + IFN-α + CXCL9 + CXCL10	Tetravalent Combination Therapy	Ph.1	Solid tumors
CaroGen Poly-vec (CARG-2020)	(VLV) **RNA-based**	IL-12 IL-17RA antagonist shRNA (PD-L1)	Trivalent Combination Therapy	Preclinical	Ovarian, CRC, HCC Other solid tumors

USE OF PROCEEDS: $25 M

Items	2021	2022	2023	Cumulative
R&D Expenses	1,132,800	2,124,000	2,289,600	5,546,400
SRA, CROs, CDMOs	2,790,000	5,520,000	7,080,000	15,390,000
G & A	421,200	1,068,000	1,104,000	2,593,200
Legal/patent/Accounting/Rent	319,000	550,000	550,000	1,419,000
Total	4,663,000	9,262,000	11,023,600	24,948,600