Developing Novel Immunotherapies For Solid Tumors and Infectious Diseases

Bijan Almassian, PhD
CEO
AVIDIO Platform & Pipeline

**Platform:** AVIDIO (Artificial Virus for Infectious Diseases and Immuno-Oncology) 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)
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

Source: Rose et al. PNAS (2014) 111:16866-71
CARG-2020: Oncolytic Platform Designed to Target Multiple Pathways

Rationale:

<table>
<thead>
<tr>
<th>IL-12</th>
<th>Amplify anti-cancer immune response</th>
</tr>
</thead>
<tbody>
<tr>
<td>IL-17RA antagonist</td>
<td>Expand immune response by blocking tumor-promoting inflammation</td>
</tr>
<tr>
<td>shRNA-PD-L1</td>
<td>Sustain anti-cancer immunity by blocking immune checkpoint pathway</td>
</tr>
</tbody>
</table>

SFV nsp1-4 → IL-12 → IL-17R antagonist → shRNA-PD-L1 → VSV-G
CARG-2020 Intravenously Inhibits Tumor Growth Significantly in Syngeneic Mouse MC38 Colon Cancer Model

Injection dose: $1 \times 10^8$ PFU per mouse per dose, IV
CARG-2020 Intratumorally Reduces Tumor Growth Significantly in MC38 Colon Cancer Model

VLV treatment: $5 \times 10^7$ PFU per dose, IT

Days of injection

Days after tumor challenge
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.
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.

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

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

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

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

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

day 3

day 17

day 27

* start of treatment
CARG-2020 (TRIVALENT) BLOCKS TUMOR RECURRENCE AND EXTENDS OVERALL SURVIVAL

Injection Days 3, 5 and 7
Control: PBS

* p = 0.0011
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 is delivering transgenes for three HBV antigens (MHBs, HBc and polymerase):

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

\textbf{VLV Platform and HBV Publications:}

- Rose et al. \textit{PNAS} (2014) 111:16866
- Chiale et al. \textit{Vaccines} (2020) 8:279
CARG-301 PRIME-BOOST SIGNIFICANTLY REDUCES HBsAG IN MICE WITH HIGH HBV ANTIGEN LEVELS

CARG-GFP
CARG-201
CARG-301

Prime
Boost 1
Boost 2

2 HBV antigens
3 HBV antigens

HBsAg ng/mL

Week

0 1000 2000 3000 4000

-1 1 3 5 7 9 11 14 17

HBsAg ng/mL

Week post-AVIDIO start

0 2000 4000 6000

-1 1 3 5 7 9 11 14 17
CARG-301(HBV) DEVELOPMENT PLAN: TIMELINE, BUDGET & DELIVERABLES

- **Lead Vaccine Optimization**
- **Animal Efficacy Studies**
- **GMP Manufacturing**
- **GLP Safety**
- **IND Filing**
- **Phase I Human Clinical Trials 1a & 1b**
AVIDIO is Safe

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

Composition of Matter: *Evolution of High-Titer Virus-Like Vesicles for Vaccine Applications*
  - 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*
  - National Phase, November 15, 2016
  - US, EU, China, India, Australia, Brazil, Canada, Japan

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

Protein X or RNAs

Infection

STEP 1: VLV infects a target cell

VLV or AVIDIO

STEP 2: VLV RNA enters target cell and produces X

STEP 3: Promotes broad immunotherapeutic effects

Expression

Protein X or RNAs

Antitumor and Antiviral Responses

STEP 1: VLV infects a target cell

VLV or AVIDIO

STEP 2: VLV RNA enters target cell and produces X

STEP 3: Promotes broad immunotherapeutic effects

Expression

Protein X or RNAs

Antitumor and Antiviral Responses

VLV-G
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

Secondary tumor on contralateral flank

Tumor volume (mm^3)

D6  D8  D10  D12  D14  D16  D18  D20  D22  D24
0   750.  1500.  2250.  3000.  3750.

Arrows indicate days of treatment

Injection on right flank of mouse
No injection treatment

No injection on contralateral (opposite) flank
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
CARG-2020 Reduces Recurrence of Chemo-resistant Tumors in Dose-dependent Manner
<table>
<thead>
<tr>
<th>Company/Drug</th>
<th>Oncolytic Vector</th>
<th>Gene Target</th>
<th>Therapy</th>
<th>Stage of Development</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Amgen</strong> T-Vec</td>
<td>HSV DNA-based</td>
<td>GM-CSF</td>
<td>Single/monotherapy</td>
<td>Licensed 2015</td>
<td>Melanoma</td>
</tr>
<tr>
<td><strong>SillaJen Inc (S.Korea)</strong> Pexa-vec</td>
<td>VAV DNA-based</td>
<td>GM-CSF</td>
<td>GM-CSF ---→ Single Pexa-vec+chemo ---→ Combo Pexa-vec+mabs ---→ Combo</td>
<td>Ph.2 Ph.1 Ph.1</td>
<td>Renal cell carcinoma, Melanoma, CRC, Solid tumors.</td>
</tr>
<tr>
<td><strong>Genelux</strong> Olvi-vec</td>
<td>VAV DNA-based</td>
<td>Olvi-vec + chemo ---→ Combo Olvi-vec + mabs ---→ Combo</td>
<td>Ph.2 Ph.1</td>
<td>Ovarian cancer, Cervical, Various cancers</td>
<td></td>
</tr>
<tr>
<td><strong>TILT Bio (Finland)</strong> TILT</td>
<td>Adenovirus DNA-based</td>
<td>TNFα + IL-12 or CD40L</td>
<td>TILT + α-PD-L1 mab ---→ Combo TILT + α-PD-1 mab ---→ Combo</td>
<td>IND ---→ Ph.1</td>
<td>Ovarian, Solid tumors</td>
</tr>
<tr>
<td><strong>PsiOxus (U.K.)</strong> NG-641</td>
<td>Adenovirus DNA-based</td>
<td>FAP-Tac + IFN-α + CXCL9 + CXCL10</td>
<td>Tetravalent Combination Therapy</td>
<td>Ph.1</td>
<td>Solid tumors</td>
</tr>
<tr>
<td><strong>CaroGen</strong> Poly-vec (CARG-2020)</td>
<td>(VLV) RNA-based</td>
<td>IL-12 IL-17RA antagonist shRNA (PD-L1)</td>
<td>Trivalent Combination Therapy</td>
<td>Preclinical</td>
<td>Ovarian, CRC, HCC Other solid tumors</td>
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</table>
# USE OF PROCEEDS: $25 M

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