



# Corporate Overview

March 2025



# FORWARD LOOKING STATEMENTS

*This presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. In some cases forward-looking statements can be identified by terminology such as “may,” “should,” “potential,” “continue,” “expects,” “anticipates,” “intends,” “plans,” “believes,” “estimates,” and similar expressions, and include statements regarding topline data expected in Q2 2025; cash runway into Q3 2025; the outcomes of a second Data Monitoring Committee review of safety data from the VIRAGE Phase 2b clinical trial of VCN-01 in metastatic pancreatic ductal adenocarcinoma expected in Q2 2025 ; having clear direction on the path forward to a potential pivotal trial for VCN-01 in PDAC should the VIRAGE Phase 2b trial be successful; the potential pivotal Phase 3 clinical study of lead clinical candidate VCN-01 in combination with standard-of-care chemotherapy gemcitabine/nab-paclitaxel for the treatment of metastatic PDAC; an End-of-Phase 2 meeting with the FDA to discuss the proposed Phase 3 study being requested before the end of 2025; preparing the clinical study report from the investigator sponsored Phase 1 trial of intravitreal VCN-01 in pediatric patients with refractory retinoblastoma conducted at Sant Joan de Déu-Barcelona Children’s Hospital; continuing discussions with key opinion leaders for developing a potential pivotal trial protocol for retinoblastoma; obtaining grant funding or finding a licensee or partner for the SYN-004 development program; the THERICEL project establishing the viability of using Theriva’s proprietary A549 suspension cells for the clinical manufacture of adenoviral and AAV therapies; anticipated increase in research and development expense as the Company completes its VIRAGE Phase 2 clinical trial of VCN-01 and plans for its Phase 3 clinical trial of VCN-01 in PDAC, advances its VCN-01 program in retinoblastoma, expands GMP scale-up manufacturing activities for VCN-01, and continues supporting its other preclinical and discovery initiatives. Important factors that could cause actual results to differ materially from current expectations include, among others, the topline data being positive for the VIRAGE Phase 2b clinical trial of VCN-01 in metastatic pancreatic ductal adenocarcinoma; Company’s ability to effectively design the pivotal trial for VCN-01 in PDAC; the Company’s and VCN’s ability to reach clinical milestones when anticipated, including the ability to continue to enroll patients as planned, generating positive clinical data when anticipated (including from the VIRAGE Phase 2b clinical trial of VCN-01 in metastatic pancreatic ductal adenocarcinoma) that establishes VCN-01 may lead to improved clinical outcomes for patients with PDAC and other solid cancers; the Company’s and VCN’s product candidates demonstrating safety and effectiveness, as well as results that are consistent with prior results; the Company’s ability to complete clinical trials on time and achieve the desired results and benefits; the Company’s ability to obtain regulatory approval for commercialization of product candidates or to comply with ongoing regulatory requirements; regulatory limitations relating to the Company’s and VCN’s ability to promote or commercialize their product candidates for the specific indications; acceptance of product candidates in the marketplace and the successful development, marketing or sale of the Company’s and VCN’s products; developments by competitors that render such products obsolete or non-competitive; the Company’s and VCN’s ability to maintain license agreements; the continued maintenance and growth of the Company’s and VCN’s patent estate; the ability to continue to remain well financed; the ability to find licensees and grant funding for the SYN-004 development program and other factors described in the Company’s Annual Report on Form 10-K for the year ended December 31, 2024 and its other filings with the SEC, including subsequent periodic reports on Forms 10-Q and current reports on Form 8-K. The information in this release is provided only as of the date of this release, and Theriva Biologics undertakes no obligation to update any forward-looking statements contained in this release on account of new information, future events, or otherwise, except as required by law.*

# OVERVIEW

- **Theriva Biologics** is developing unique oncolytic viruses optimized for systemic administration
- **VCN-01** Completed enrollment in a Phase 2b clinical trial in first-line metastatic pancreatic cancer in combination with SoC chemotherapy with topline data expected Q2 2025
- **VCN-01** Phase 1 clinical trials support multiple additional indications (retinoblastoma, HNSCC, CRC) and combinations (immunotherapies)
- **Albumin Shieldz / VCN-X** platform and innovative oncolytic virus discovery engine enable development of a distinct product pipeline

## Financial Snapshot

Exchange	NYSE American
Ticker	TOVX
<b>Cash (12/31/2024)</b>	<b>\$11.6M</b>
Projected cash runway	Q3 2025
Average Daily Volume (3M Ave)	461.3k <sup>1</sup>
Locations	Rockville, MD Barcelona, Spain

# SEASONED LEADERSHIP TEAM



## Steven Shallcross

Chief Executive Officer, Chief Financial Officer

Served as the Company's CEO since 2018 and CFO since joining the Company in 2015

Deep operational, financial and international biotech industry experience and proven track record of leading the financial development and strategy in the public sector

Senseonics

VANDA  
PHARMACEUTICALS INC.

Innocoll

NUO  
THERAPEUTICS

Theriva  
BIOLOGICS



## Manel Cascalló PhD

General Director, EU Subsidiary

Expertise in oncolytic adenovirus development, received several the use of adenovirus as antitumoral agents and authored many peer-scientific publications

Deep regulatory experience and as an independent expert for the European Medicines Agencies (EMA)

VCN  
BIOSCIENCES



## Vince Wachter PhD

Head Corporate Development

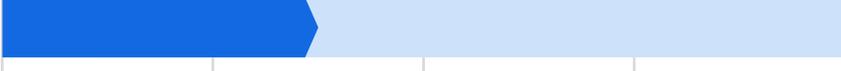
Nearly 30 years leading corporate strategy, partnering, research, clinical development, and intellectual property programs for start-ups, small companies, and new business units within large companies

Development experience across oncology, infection, GI, metabolic diseases, transplantation, and drug delivery

EASTMAN

Verva  
Pharmaceuticals

# THERIVA PIPELINE

Candidate	Target	Pre-IND	Phase 1	Phase 2	Phase 3	Collaborators	Status*	
<b>VCN-01</b> Selective, Stroma Degrading OV	Pancreatic Cancer (IV) with gemcitabine/nab-paclitaxel							<b>Phase 2b Study On-going</b> Orphan Drug Designation US, EU Fast Track Designation US
	Retinoblastoma (IVit)							<b>Phase 1 Complete, CSR in preparation</b> Orphan Drug Designation US, EU Rare Pediatric Disease Designation US
	HNSCC (IV) + durvalumab							<b>Phase 1 Complete, CSR in preparation</b>
	Brain Tumors							<b>Phase 1 Study On-going</b>
<b>VCN-X and Albumin Shield OVs</b>	Solid tumors (IV)							<b>Preclinical Studies On-going</b>
<b>SYN-004</b> [1,2] Oral $\beta$ -lactamase	<b>Prevention of aGVHD in allo-HCT</b>							<b>Phase 1b/2a On-going</b>
<b>SYN-020</b> Oral IAP	<b>Potential indications include NAFLD/NASH, celiac, radiation enteritis</b>							<b>Phase 1 Studies Complete</b>

# VCN-01 IS A UNIQUELY ENGINEERED HUMAN ADENOVIRUS 5

Systemic

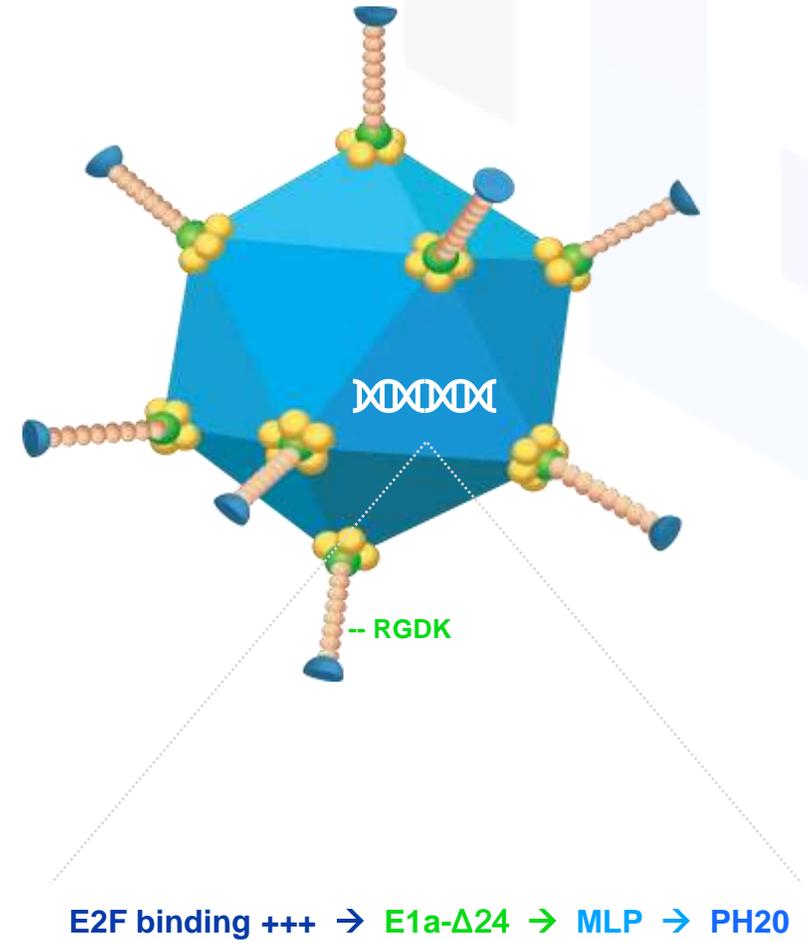
Access primary and **metastatic** lesions  
High dose, highly replicating

Selective

Replicates only in **tumor** cells  
Liver detargeted

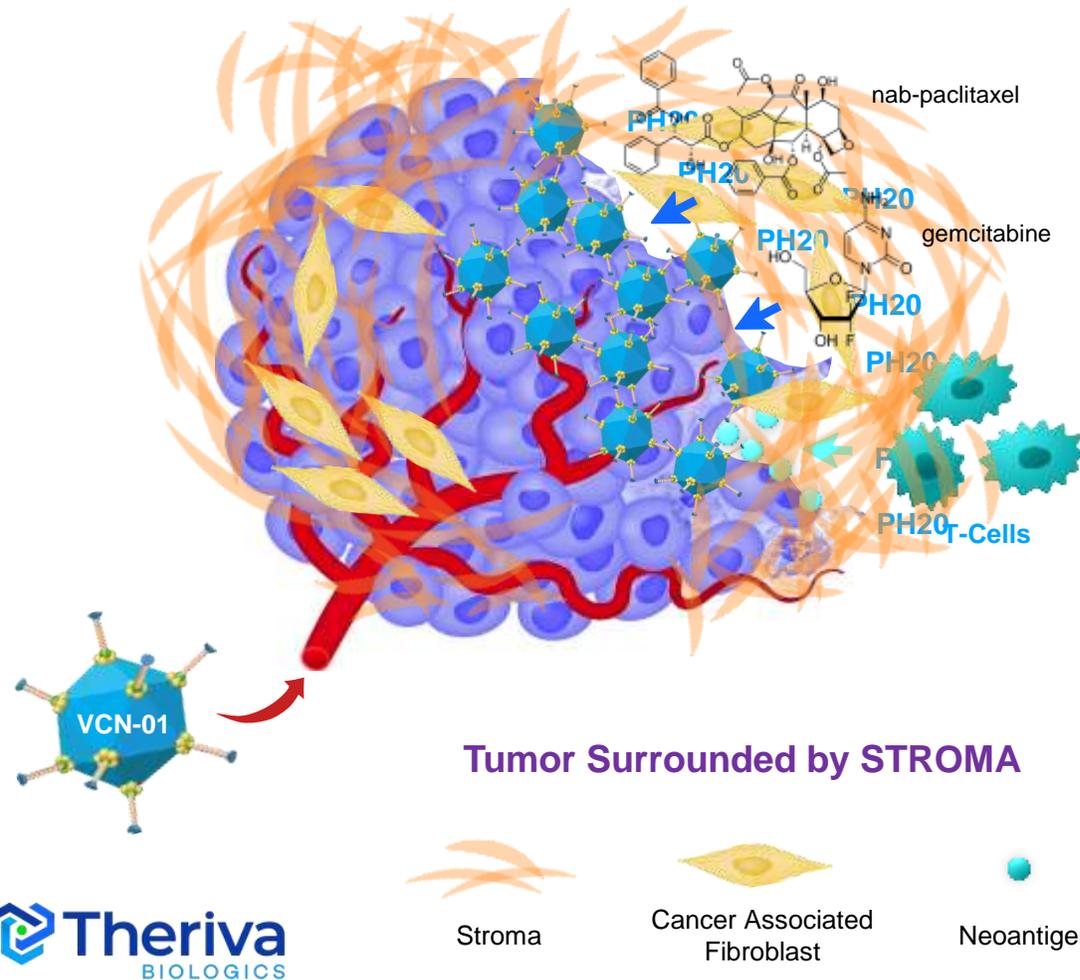
Stroma Degrading

Expresses **PH20** (hyaluronidase)  
after viral replication cycle



# VCN-01 IS A UNIQUELY ENGINEERED HUMAN ADENOVIRUS 5

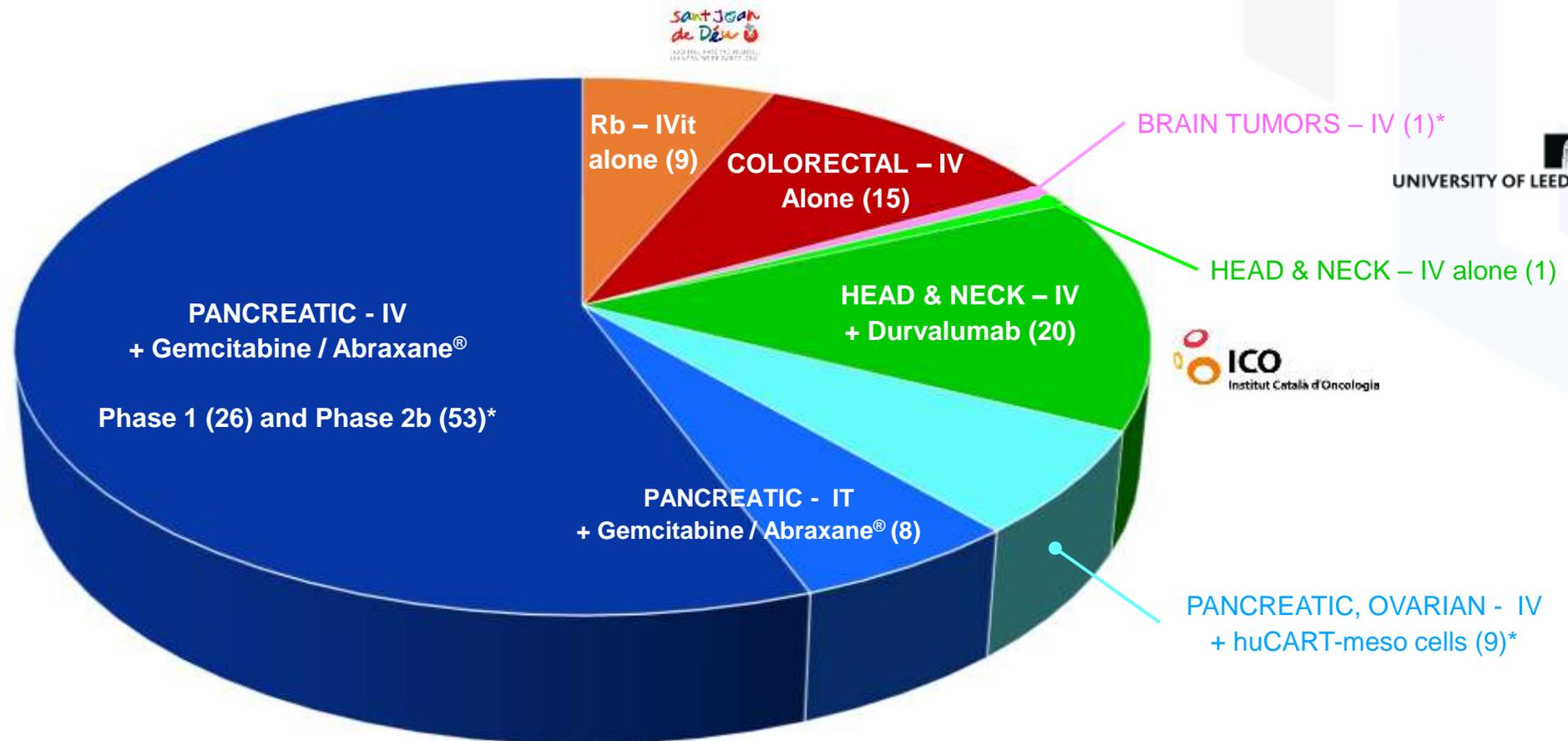
## Designed to have multiple anti-tumor actions



- 1** **SYSTEMIC** administration enables VCN-01 access to primary tumor and metastases and detargets the liver
- 2** **SELECTIVE** replication at very high levels lyses tumor cells directly without harming healthy tissues
- 3** **STROMA** degradation by PH20 facilitates tumor access and destruction by coadministered cancer therapies
- 4** **IMMUNOGENIC** actions of VCN-01 turn “cold” tumors “hot” and elicit an anti-tumor immune response

# VCN-01 EXTENSIVE CLINICAL PROGRAM

142 patients treated with VCN-01 to date in multiple indications and combinations

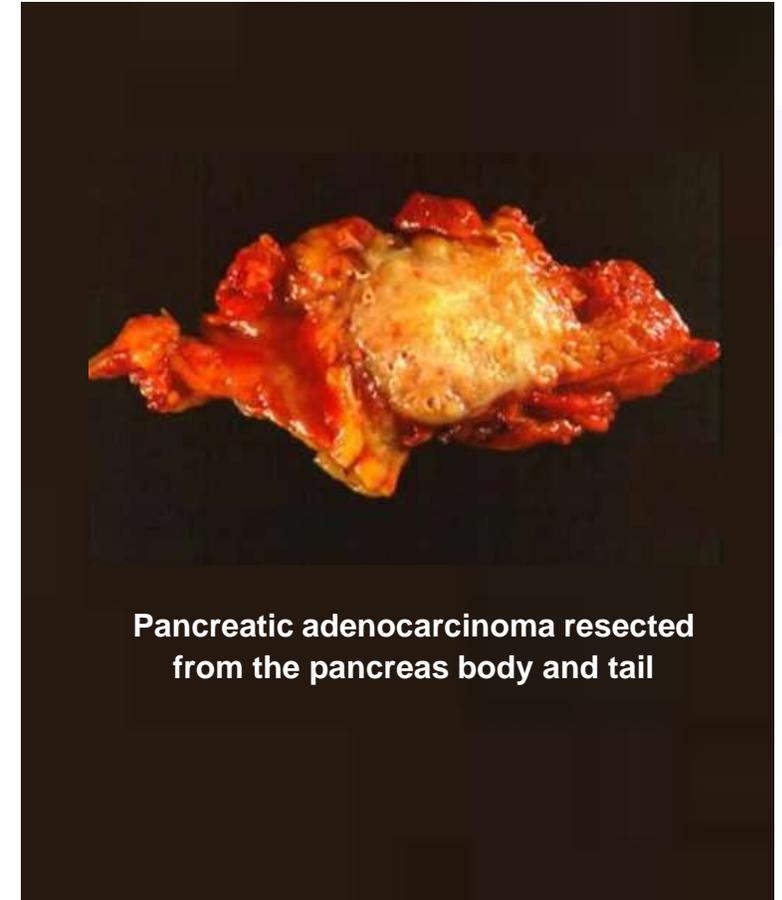


(Number of VCN-01 Patients Treated in Parentheses)

# VCN-01 LEAD INDICATION PANCREATIC CANCER

Highly fatal cancer protected by dense tumor stroma

- Orphan disease with the highest mortality of all solid tumors
  - Median survival 8-11 months for metastatic disease<sup>1,2</sup>
  - USA est. 66,440 new cases and 51,750 deaths in 2024<sup>3</sup>
- **Hyaluronic acid** in stroma is associated with reduced treatment efficacy and poor prognosis<sup>4</sup>
  - VCN-01 designed to degrade hyaluronic acid
- Incidence is growing worldwide
  - Est. treatment market ~\$2.5B (2022) ~\$7.0B (2030)<sup>5</sup>



# VCN-01 FAVORABLE OUTCOMES IN PHASE 1 TRIAL

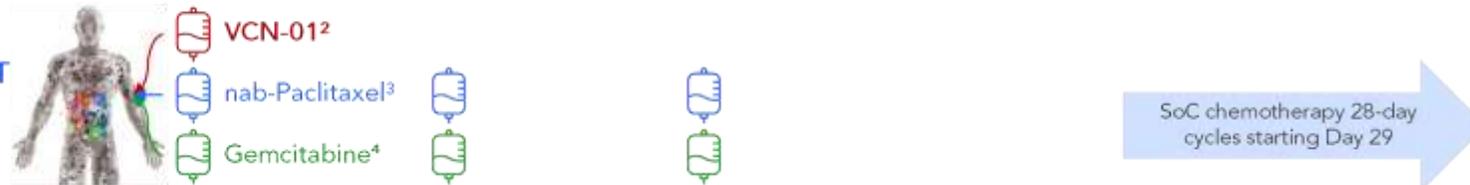
Multicenter, open-label, dose escalation study (NCT02045602)

**ARM I  
MONOTHERAPY**  
Solid tumors (16)

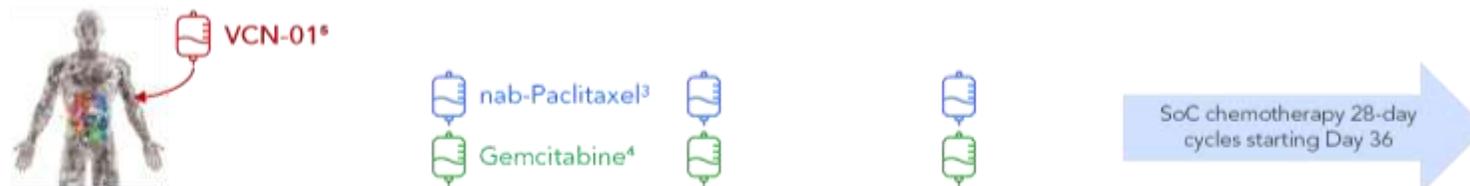


- ✓ Single IV doses of VCN-01 alone or with standard-of-care (SoC) chemotherapy gemcitabine/nab-paclitaxel (Abraxane®)
- ✓ Evaluate safety and tolerability, recommended Phase 2 dose

**ARM II  
CONCOMITANT**  
PDAC (12)



**ARM III  
SEQUENTIAL**  
PDAC (14)



Cycle 1 Day 1 8 15 22 29 36

# VCN-01 FAVORABLE OUTCOMES IN PHASE 1 TRIAL

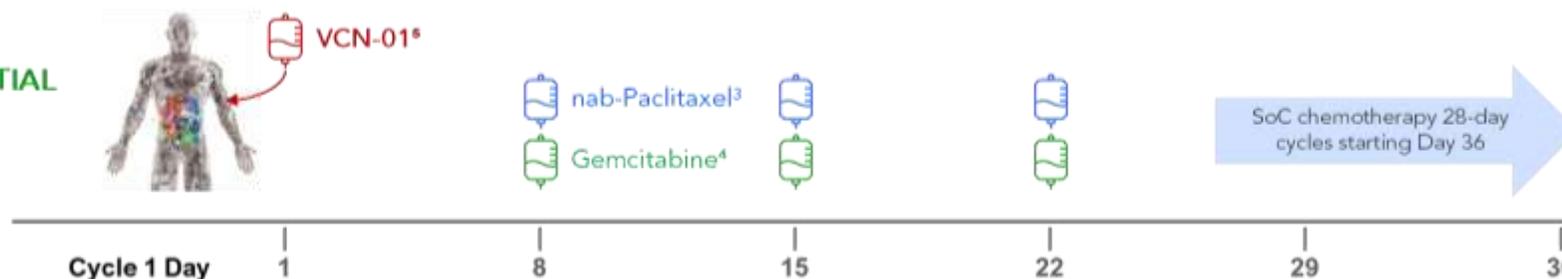
Multicenter, open-label, dose escalation study (NCT02045602)

OUTCOME	VCN-01 DOSE, virus particles (n) <sup>1</sup>			SoC ALONE <sup>2</sup>
	3.3x10 <sup>12</sup> (6)	1.0x10 <sup>13</sup> (6)	Combined (12)	Phase 3 (431)
Responders, %	16.7%	<b>83.3%</b>	50.0%	22.9%
Median OS, months	13.1	<b>20.8</b>	13.5	8.5
Median PFS, months	9.9	6.3	6.7	5.5
Survival ≥12 months	.	.	67%	35%

RELATED AEs IN ≥1 PATIENT <sup>1</sup>	CTCAE SEVERITY	
	VCN-01 Combined, Sequential Regimen	Grade 1-2
<b>Pyrexia/Influenza-like Illness</b>	<b>12 (85.7%)</b>	-
Nausea	3 (21.4%)	-
Vomiting	3 (21.4%)	-
Asthenia/Fatigue	3 (21.4%)	-
Transaminase increases (ALT, AST)	2 (14.3%)	2 (14.3%)
Thrombocytopenia	2 (14.3%)	-

KOLs advise that Hazard Ratio <0.7 is a significant patient outcome

ARM III  
SEQUENTIAL  
PDAC (14)



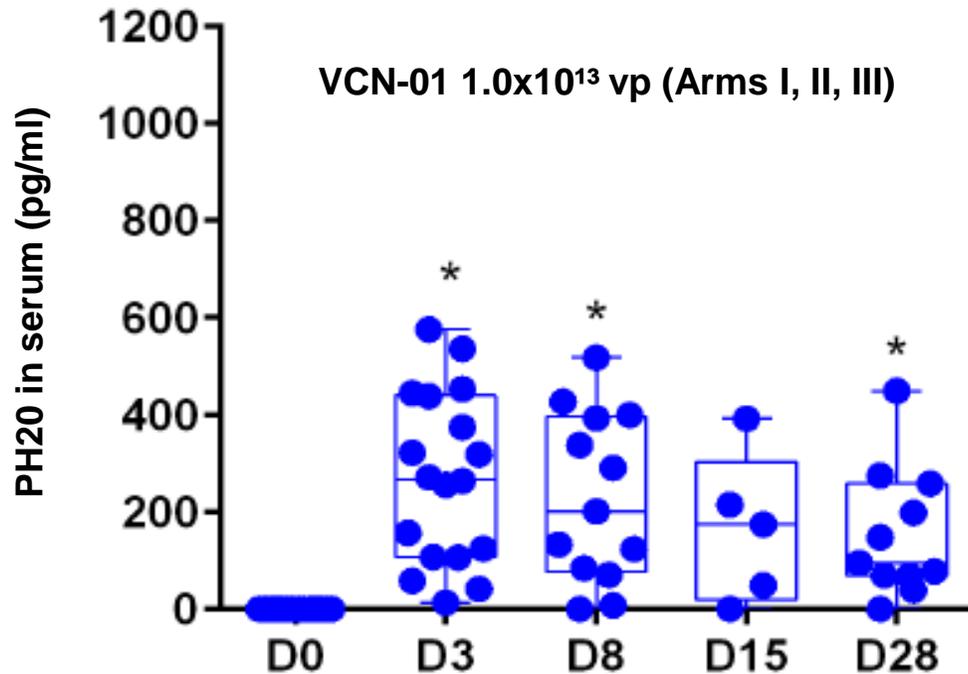
<sup>1</sup>Single dose of VCN-01 (1x10<sup>11</sup> to 1x10<sup>13</sup> vp/dose) administered by 10 min IV infusion. <sup>2</sup>VCN-01 doses 3.3x10<sup>12</sup> vp (n=6) and 1x10<sup>13</sup> vp (6).

<sup>3</sup>nab-Paclitaxel (Abraxane®; 30 min infusion) administered at least 4 hours after VCN-01. <sup>4</sup>Gemcitabine (30 min infusion) administered immediately after Abraxane® infusion. <sup>5</sup>VCN-01 doses 3.3x10<sup>12</sup> vp (8) 1x10<sup>13</sup> vp (6). Garcia-Carbonero (2022) J Immunother Cancer 10:e003255.

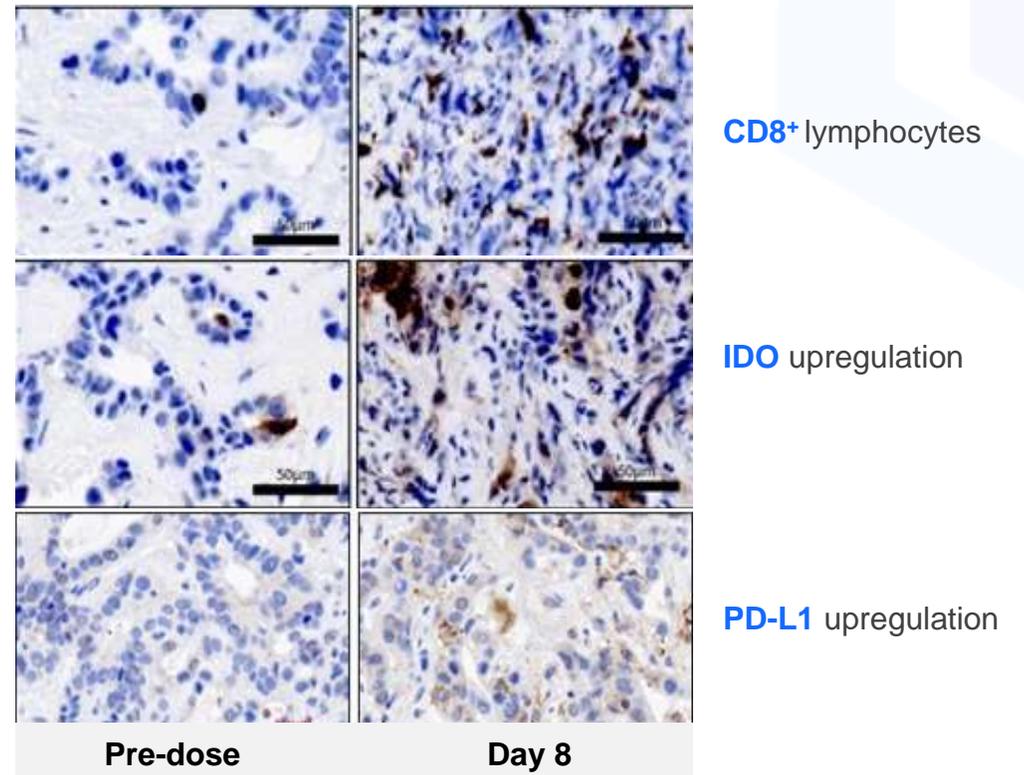
# CLINICAL DATA SUPPORT VCN-01 MODE-OF-ACTION

## Remodels the tumor matrix and turns “cold” tumors “hot”

**Persistent replication:** PH20 levels in patient sera indicate sustained VCN-01 activity in tumors



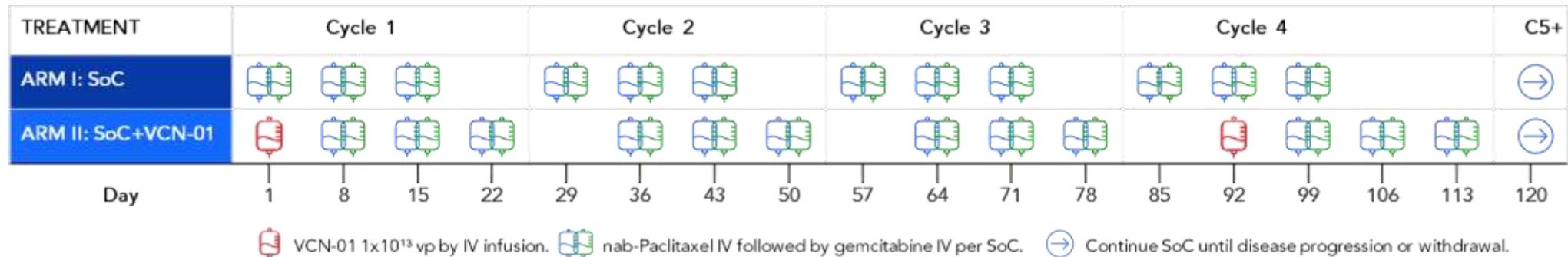
Immune markers upregulated in biopsies of **hepatic metastases**



# VIRAGE PHASE 2B CLINICAL TRIAL in PANCREATIC CANCER

Multicenter, open-label, randomized, controlled trial (NCT05673811)

- Evaluating **first-line** treatment of patients with metastatic pancreatic ductal adenocarcinoma (PDAC)
  - Randomized 1:1 to receive gemcitabine/nab-paclitaxel SoC or up to **two doses** of VCN-01 plus SoC
  - Primary endpoints **overall survival**, VCN-01 safety and tolerability
  - Secondary endpoints include **response rates**, progression free survival, landmark survival
- **Achieved** target of 92 patients (46 in each arm) enrolled at sites in Spain and the USA
  - Following last patients for survival



# VCN-01 DEVELOPMENT IN PANCREATIC CANCER

- Completed enrollment into the VIRAGE Study Q3 2024
  - First DMC safety review completed Q1 2024 - Second DMC scheduled Q1 2025
  - No safety concerns were raised, and no protocol amendments were requested
- Topline date expected Q2 2025
- Orphan Drug Designation to facilitate regulatory interactions and provide market exclusivity
- Fast Track Designation
- On-going discussions with regulatory agencies about potential pivotal clinical trial design
  - AEMPS, FDA, EMA
- Evaluating potential expansion opportunities in pancreatic cancer<sup>1</sup>
  - Combination with FOLFIRINOX or NALIRIFOX<sup>2</sup>

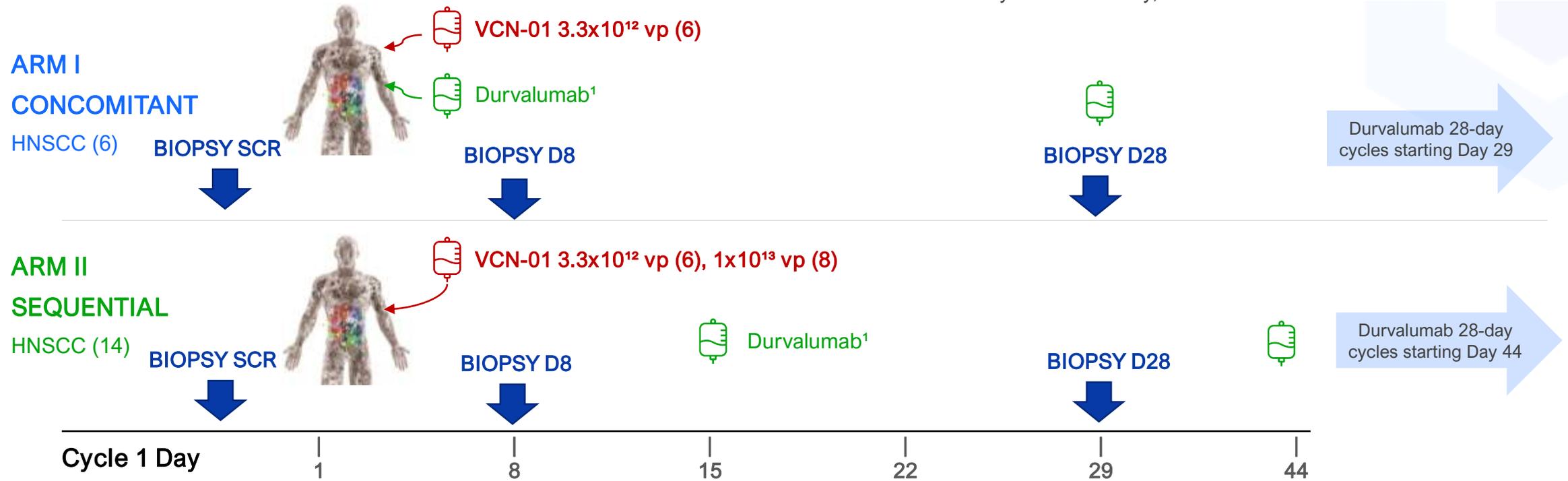


## VCN-01 IN HEAD & NECK CANCER

# VCN-01 IV + ANTI-PD-L1 PHASE 1 TRIAL in HNSCC

## Multicenter, open-label, dose escalation study (NCT03799744)

- ✓ Single IV doses of VCN-01 combined with anti-PD-L1
- ✓ Patients with metastatic squamous cell carcinoma of the head & neck previously **REFRACTORY** to anti-PD(L)1 treatment (R/M HNSCC)
- ✓ Evaluate safety and tolerability, recommended Phase 2 dose



# EXTENDED SURVIVAL with VCN-01+DURVALUMAB

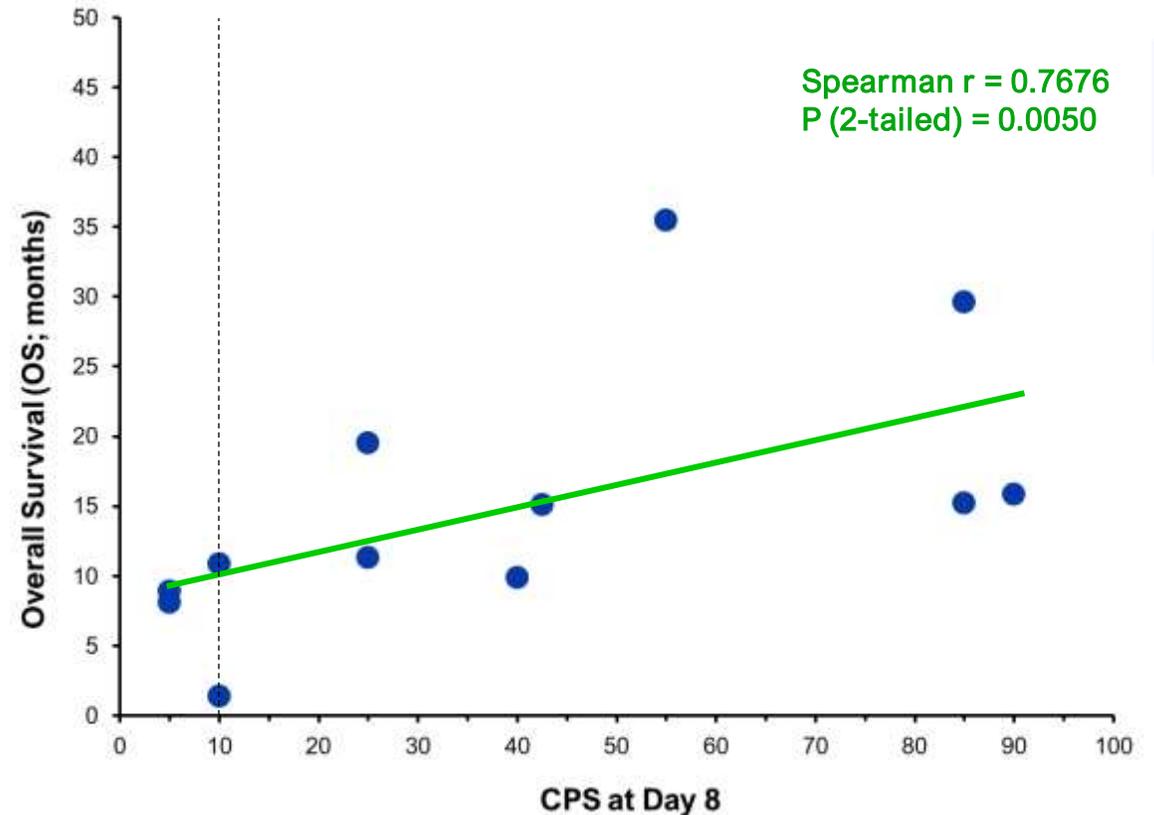
## Survival correlated with PD-L1 upregulation after VCN-01 treatment

- Higher than expected survival (OS) despite previous anti-PD(L)1 failure

Regimen	Median OS (95% CI), mos	
	3.3x10 <sup>12</sup> vp	1.0x10 <sup>13</sup> vp
Concomitant	10.4 (8.9-NE)	..
Sequential	15.5 (15.1-NE)	17.3 (11.3-NE)

- No correlation of survival with baseline tumor PD-L1 expression (CPS) BUT significant correlation of survival with CPS 8-days after VCN-01 treatment

Overall Survival vs CPS in Biopsies at Day 8



# VCN-01 FINDINGS in R/M HNSCC

## Data support VCN-01 MOA and immune enhancing effects

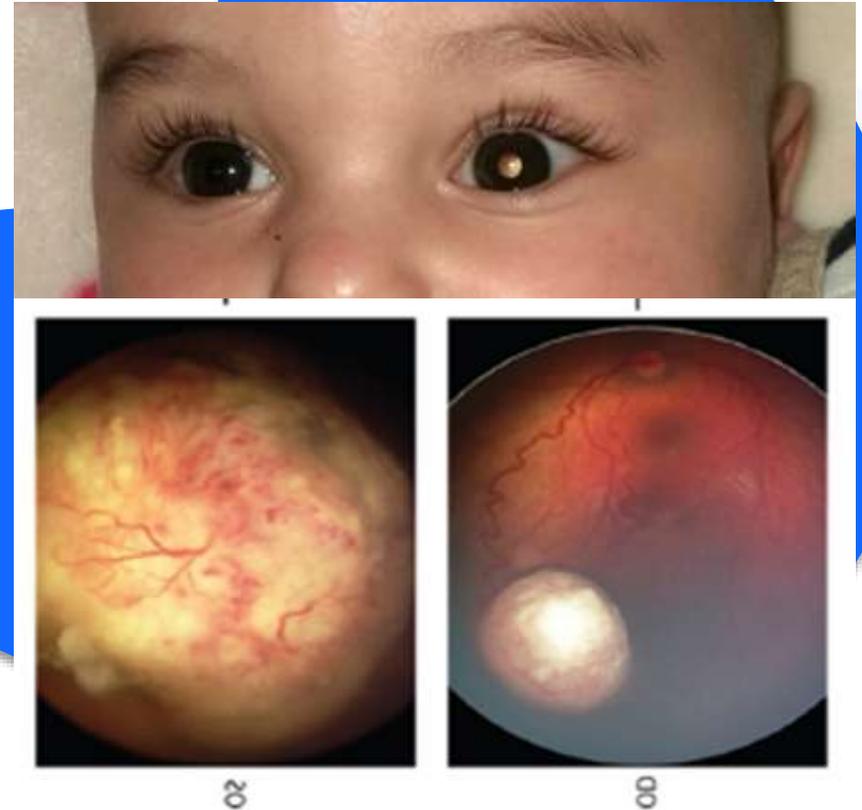
- VCN-01 has an acceptable adverse event profile when administered prior to durvalumab (Imfinzi®)
- VCN-01 reaches tumors, has sustained replication and PH20 expression
- VCN-01 treatment led to downregulation of tumor matrix genes and increased levels of immune markers in tumor biopsies (CD8, PD-L1, IDO)
- VCN-01-treated patients showed **increased response** to subsequent chemotherapy treatment lines after progressing on this trial

VCN-01 IN RETINOBLASTOMA



# RETINOBLASTOMA, A RARE PEDIATRIC MALIGNANCY

- Retinoblastoma (Rb) is an orphan indication that accounts for ~2-3% of all childhood cancers<sup>1</sup>
- 200-300 cases each year in the USA, EU<sup>2-4</sup>
- VCN-01 selectivity enables development as an intravitreal treatment for Rb patients
- VCN-01 could be used in combination with chemotherapy to potentially improve outcomes
- VCN-01 could be used as a rescue therapy for patients who fail standard therapy

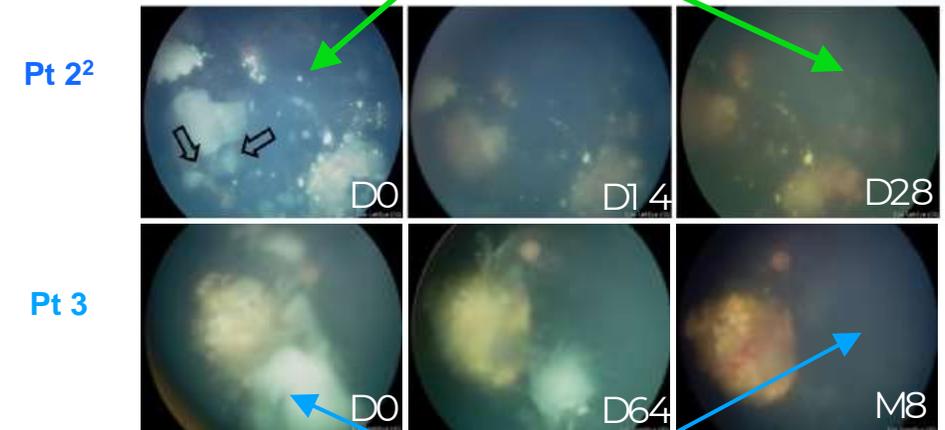


# VCN-01 IN RETINOBLASTOMA

- Single center, open-label, dose escalation study of intravitreal (IVit) VCN-01<sup>1-3</sup>
  - Children aged 1-12 years (n=9)
  - Retinoblastoma that is recurrent or refractory to chemotherapy and for whom enucleation is the best treatment option
  - VCN-01 doses of  $2.0 \times 10^9$  vp per eye (n=1) or  $2.0 \times 10^{10}$  vp per eye (n=8) on days 1 and 15
- Promising antitumor activity and appropriate adverse event profile and tolerability at RP2D
  - Reduction of vitreous seeds in 3 patients of 6 evaluable patients
  - Enucleation avoided in 2 patients; low VCN-01 dose and/or damage from prior chemotherapy meant the eye could not be saved in 4 patients
- Earlier VCN-01 intervention anticipated to have better outcomes

## Promising Results in Patients Treated with High Dose VCN-01

Reduced number and size of tumor vitreous seeds following VCN-01 administration<sup>2</sup>



Complete tumor regression<sup>3</sup>

# INTERIM ADVERSE EVENT DATA FOR INTRAVITREAL VCN-01

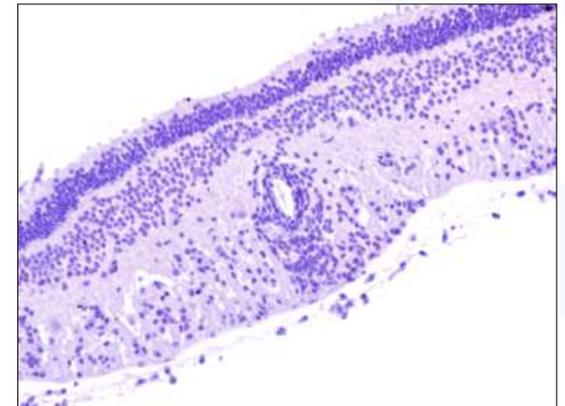
Two Intravitreal VCN-01 Doses of  $2.0 \times 10^9$  or  $2.0 \times 10^{10}$  vp per eye<sup>1</sup>

Adverse Reaction	Pts	All Grades		Grade $\geq 3$	
CTCAE grade	N	n	%	n	%
Uveitis	6	2	33%	2	33%
Eye oedema	6	1	17%	0	0%
Conjunctival hyperemia	6	1	17%	0	0%
Eye inflammation	6	1	17%	0	0%

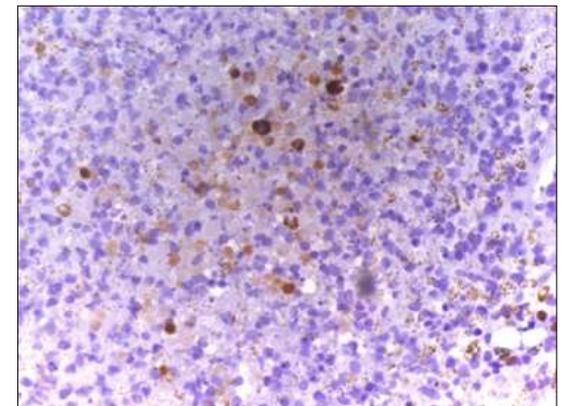
## Selective expression of viral proteins

- VCN-01 was reasonably well tolerated after intravitreal administration<sup>2</sup>, although some turbidity and uveitis associated with intravitreal inflammation was observed
- Intravitreal inflammation was managed with local and systemic administration of anti-inflammatory drugs
- VCN-01 induced reversible changes in the electroretinograms but didn't impact visual acuity
- VCN-01 does not replicate in healthy retinal tissue of patients with either somatic or germline Rb mutation<sup>3</sup>

*Conserved retina*



*Necrotic tumor*



# VCN-01 DEVELOPMENT IN RETINOBLASTOMA

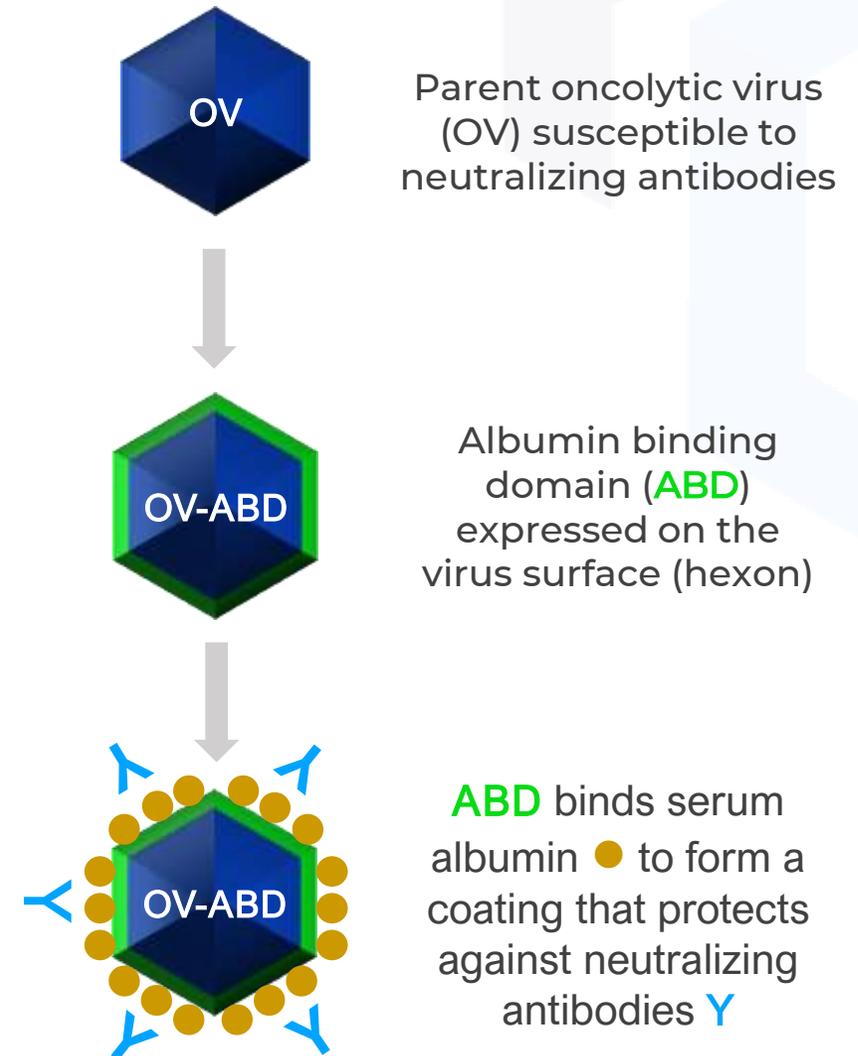
- Phase 1 ISS Completed H1 2024
  - Initial data demonstrate acceptable adverse event profile and one durable complete response
- Developing a clinical protocol for an open-label, multinational study
  - Retinoblastoma patients with vitreous seeds
  - IVit VCN-01 in combination with chemotherapy (no defined SoC)
  - PI Dr. Guillermo Chantada, MD PhD<sup>1</sup>
- Status
  - US and EU Orphan Drug Designation
  - Pre-IND meeting with FDA completed Q4 2023
  - Rare Pediatric Disease Designation (potential eligibility for Priority Review Voucher)

VCN-X NEXT GENERATION  
OV DISCOVERY PLATFORM



# ALBUMIN SHIELDz to ENHANCE OV SYSTEMIC DELIVERY

- Albumin Shield technology protects OVs as they travel to tumors after systemic administration<sup>1,2</sup>
- Albumin Shield modified OVs bind albumin in the patient's blood to form a protective coating
- Albumin Shield genetic modification allows parent and progeny virus to be albumin coated
- Albumin Shield may enable **multiple IV administrations** for hard-to-treat patients
- Albumin Shield first candidate VCN-11 is being prepared for a potential Phase 1 clinical trial



# THERIVA OV PIPELINE DISCOVERY AND DEVELOPMENT

Advancing founders' decade of world leading OV innovation

## Common Features

Clinically-tested Adenovirus Expressing PH20  
Hyaluronidase to Degrade Stroma

+

Albumin Shieldz To Prevent Neutralization by  
anti-viral Antibodies and Facilitate IV Multidosing

+

Unique Multifunctional Proteins to Turn Cold Tumors  
Hot and Enhance Anti-tumor Immune Response

## Product Specific Features



**VCN-11 Hyaluronidase alone**



**VCN-12 Hyaluronidase + Toxins**



**VCN-13 Fusion Hyaluronidase + scPD-L1**



**VCN-XX Hyaluronidase + other payloads**

# ACHIEVEMENTS AND PROJECTED MILESTONES

**VCN-01 PDAC FDA Type D**  
*potential Phase 3 study design*

**VCN-01 EMA Sci Advice**  
*potential Phase 3 study design*

**VIRAGE Topline Data**  
*contingent on patient survival*

**VCN-01 PDAC CMC**  
*if regulatory agreement<sup>1</sup>*

**VCN-01 Rb ODD from EMA**  
*Retinoblastoma*

**VCN-01 Rb Presentation**  
*abstract submitted to ASCO*

**VCN-01 Rb Phase 2 design**  
*if regulatory agreement<sup>1</sup>*

**SYN-004 in allo-HCT**  
DSMC positive review

**VCN-12 candidate selection**  
*next generation OV<sup>2</sup>*

**THERICEL**  
*proprietary suspension cell line*

Q3-4 2024

Q1 2025

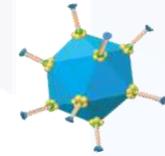
Q2 2025

Q3-Q4 2025

# THERIVA OV PORTFOLIO HIGHLIGHTS

## Unique MOA enables multiple indications and combinations

- Highly differentiated OVs designed to have multiple antitumor effects
  - Systemic administration, selective tumor replication, stroma degradation
  - Designed to increase cell lysis, tumor immunogenicity, and tumor access by co-administered therapies
- Multiple potential value opportunities for lead asset VCN-01
  - Different indications (PDAC, HNSCC, retinoblastoma)
  - Diverse combinations (chemotherapy, CPI, CAR-T)
- Regulatory status expected to facilitate VCN-01 development
  - PDAC: Orphan Drug Designation (FDA, EMA), Fast Track designation (FDA)
  - Retinoblastoma: Orphan Drug Designation (EMA; FDA); Rare Pediatric Disease Designation (FDA: potential access to priority review voucher)
- Leading OV discovery engine advancing diverse new product candidates
  - Potent tumor killing with potential single agent efficacy



Appendix



# VCN-01 COMPARED TO OTHER ONCOLYTIC VIRUSES IN DEVELOPMENT

COMPANY	THERIVA BIOLOGICS	CG ONCOLOGY	GENELUX	ONCOLYTICS BIOTECH	REPLIMMUNE
Ticker	NYSE MKT: TOVX	NASDAQ: CGON	NASDAQ: GNLX	NASDAQ: ONCY	NASDAQ: REPL
Market Cap <sup>1</sup>	\$3.9M	\$2.0B	\$128.1M	\$56.6M	\$918.0M
Product	<b>VCN-01</b>	<b>CG0070</b>	<b>Olvi-Vec</b>	<b>Pelareorep</b>	<b>RP1, RP2</b>
Virus	Adenovirus 5	Adenovirus 5	Vaccinia	Reovirus	Herpes Simplex
Type	DNA	DNA	DNA (enveloped)	RNA	DNA (enveloped)
Tumor selectivity mechanism	Selective replication (Rb-E2F dysfunction)	Selective replication (Rb-E2F dysfunction)	Low tumor IFN TK deletion	Low tumor IFN Ras activation	Low tumor IFN ICP34.5 deletion
Therapeutic Transgene	PH20	GM-CSF	..	..	GM-CSF, GALV-GP R(-), anti-CTLA-4
Lead Indication (Ph)	Pancreatic (2b)	Bladder (3)	Ovarian (3)	Pancreatic, GI (2b)	Melanoma (3)
Route	IV	IVESIC	IP	IV	IT
Dose	1x10 <sup>13</sup> vp <sup>2</sup>	1x10 <sup>12</sup> vp	3x10 <sup>9</sup> pfu	4.5x10 <sup>10</sup> TCID <sub>50</sub>	1x10 <sup>7</sup> pfu/mL
Stroma Degrading	Yes	No	No	No	No
Biomarker	PH20	..	β-GAL, β-GLU, GFP	..	..

# THERIVA ONCOLYTIC VIRUSES KEY PUBLICATIONS

- Bayo-Puxan N et al. (2006) Role of the putative heparan sulfate glycosaminoglycan-binding site of the adenovirus type 5 fiber shaft on liver detargeting and knob-mediated retargeting. *J Gen Virol* 87:2487–2495
- Bazan-Peregrino M et al. (2021) VCN-01 disrupts pancreatic cancer stroma and exerts antitumor effects. *J ImmunoTher Cancer* 9:e003254.
- Garcia-Carbonero R et al. (2019) Poster 5185: Systemic administration of the hyaluronidase-expressing oncolytic adenovirus VCN-01 in patients with advanced or metastatic pancreatic cancer: first-in-human clinical trial. European Society for Molecular Oncology conference ESMO, 29 September 2019.
- Garcia-Carbonero R et al. (2022) A phase I, multicenter, open-label study of intravenous VCN-01 oncolytic adenovirus with or without nab-paclitaxel plus gemcitabine in patients with advanced solid tumors *J ImmunoTher Cancer* 10:e003255
- Guedan S et al. (2010) Hyaluronidase expression by an oncolytic adenovirus enhances its intratumoral spread and suppresses tumor growth. *Mol Ther* 18:1275–1283
- Hidalgo M et al. (2019) Poster 5465: Proof of concept clinical study by EUS-guided intratumor injection of VCN-01, an oncolytic adenovirus expressing hyaluronidase in patients with pancreatic cancer. European Society for Molecular Oncology conference ESMO, 28 September 2019.
- Jove M et al. (2022) Poster 1231P: Phase I study to evaluate the safety, tolerability, and efficacy of VCN-01 in combination with durvalumab (MEDI4736) in subjects with recurrent/metastatic squamous cell carcinoma of the head and neck (R/M HNSCC) *Ann Oncol.* 33:S1112. European Society for Molecular Oncology conference ESMO 2022, 10 September 2022
- Kiyokawa M et al. (2021) Modification of extracellular matrix enhances oncolytic adenovirus Immunotherapy in glioblastoma. *Clin Cancer Res* 27:889-902
- Martínez-Vélez N et al. (2019) The oncolytic adenovirus VCN-01 as therapeutic approach against pediatric osteosarcoma. *Clin Cancer Res* 22:2217-25
- Mato-Berciano A et al. (2021) Oncolytic adenovirus with hyaluronidase activity that evades neutralizing antibodies: VCN-11. *J Control Rel* 332:517-528
- Pascual Pasto G et al. (2019) Therapeutic targeting of the RB1 pathway in retinoblastoma with the oncolytic adenovirus VCN-01. *Sci Transl Med* 11:eaat9321
- Pascual-Pasto G et al. (2021) Presentation: VCN-01 is an encouraging therapy against retinoblastoma. International Oncolytic Virus Conference IOVC2021, 07 November 2021, Sedona, AZ.
- Rodríguez-García A et al. (2015) Safety and efficacy of VCN-01, an oncolytic adenovirus combining fiber HSG-binding domain replacement with RGD and hyaluronidase expression. *Clin Cancer Res* 21:1406-18
- Rojas J et al. (2012) Improved systemic antitumor therapy with oncolytic adenoviruses by replacing the fiber shaft HSG-binding domain with RGD. *Gene Ther* 19:453–457
- Rojas J et al. (2010) Minimal RB-responsive E1A promoter modification to attain potency, selectivity, and transgene-arming capacity in oncolytic adenoviruses. 2010) *Mol Ther* 18:1960–1971
- Rojas L et al. (2016) Albumin-binding adenoviruses circumvent pre-existing neutralizing antibodies upon systemic delivery. *J Control Rel* 237:78–88

# PANCREATIC CANCER REFERENCES

## DESCRIPTION, CLASSIFICATION, STAGING, STROMA

- Balachandran VP et al. (2019) Broadening the impact of immunotherapy to pancreatic cancer: challenges and opportunities. *Gastroenterology* 156:2056-72
- Christenson ES et al. (2020) Current and emerging therapies for patients with advanced pancreatic ductal adenocarcinoma: a bright future. *Lancet Oncol* 21:e135-e145
- Orth M et al. (2019) Pancreatic ductal adenocarcinoma: biological hallmarks, current status, and future perspectives of combined modality treatment approaches. *Radiation Oncol* 14:141
- Placencio-Hickok VR et al. (2022) Hyaluronan heterogeneity in pancreatic ductal adenocarcinoma: primary tumors compared to sites of metastasis. *Pancreatol* 22:92-97
- Sarantis P et al. (2020) Pancreatic ductal adenocarcinoma: treatment hurdles, tumor microenvironment and immunotherapy. *World J Gastrointest Oncol* 12:173-181
- Tahkola K et al. (2021) Stromal hyaluronan accumulation is associated with low immune response and poor prognosis in pancreatic cancer. *Sci Rep* 11:12216
- Yu J et al. (2015) Time to progression of pancreatic ductal adenocarcinoma from low-to-high tumour stages. *Gut* 64:1783-9

## INCIDENCE

- Bengtsson A et al. (2020) The actual 5-year survivors of pancreatic ductal adenocarcinoma based on real-world data. *Sci Rep* 10:16425.
- Carioli G et al. (2021) European cancer mortality predictions for the year 2021 with focus on pancreatic and female lung cancer. *Ann Oncol* 32:478.
- da Costa WL et al. (2020) Trends in the incidence of pancreatic adenocarcinoma in all 50 United States examined through an age-period-cohort analysis. *JNCI Cancer Spectrum* 4:pkaa033
- GLOBOCAN International 2020 survey of persons 0-74 years. <https://gco.iarc.fr/today/data/factsheets/cancers/13-Pancreas-fact-sheet.pdf>
- Michael N et al. (2019) Timing of palliative care referral and aggressive cancer care toward the end-of-life in pancreatic cancer: a retrospective, single-center observational study. *BMC Palliat Care* 18:13.
- Sung H et al. (2021) Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. *CA Cancer J Clin* 71:209–249
- Ushio J et al. (2021) Pancreatic ductal adenocarcinoma: epidemiology and risk factors. *Diagnostics* 11:562

## TREATMENT

- Conroy T et al. (2011) FOLFIRINOX versus Gemcitabine for Metastatic Pancreatic Cancer. *N Engl J Med* 364:1817-25.
- Elsayed M et al. (2021) The latest advancement in pancreatic ductal adenocarcinoma therapy: a review article for the latest guidelines and novel therapies. *Biomedicines* 9:389
- Tempero MA et al. (2021) NCCN Clinical Practice Guidelines in Oncology. Pancreatic Adenocarcinoma, V2.2021. *J Natl Compr Canc Netw* 19:439-457
- Toesca DAS et al. (2018) Management of borderline resectable pancreatic cancer. *Int J Radiation Oncol Biol Phys* 100:1155-74
- Vogel A et al. (2016) Efficacy and safety profile of nab-paclitaxel plus gemcitabine in patients with metastatic pancreatic cancer treated to disease progression: a subanalysis from a phase 3 trial (MPACT). *BMC Cancer* (2016) 16:817
- Von Hoff DD et al. (2013) Increased survival in pancreatic cancer with nab-paclitaxel plus gemcitabine. *N Engl J Med* 369:1691-703

# RETINOBLASTOMA (Rb) REFERENCES

## DESCRIPTION, CLASSIFICATION, STAGING

American Academy of Ophthalmology. EyeWiki®. Retinoblastoma. <https://eyewiki.org/Retinoblastoma>

American Cancer Society. Key statistics for retinoblastoma. <https://www.cancer.org/cancer/retinoblastoma/about/key-statistics.html>

Canturk S et al. (2010) Survival of retinoblastoma in less-developed countries impact of socioeconomic and health-related indicators. Br J Ophthalmol 94:1432-6

Fabian ID et al. (2018) Classification and staging of retinoblastoma. Community Eye Health 31:11-13

Fabian ID et al. (2020) Global retinoblastoma presentation and analysis by national income level. JAMA Oncol 6:685

Tomar AS et al. (2020) Multicenter, international collaborative study for American Joint Committee on Cancer Staging of Retinoblastoma/ Part I: metastasis-associated mortality. Ophthalmology 127:1719-32

## INCIDENCE

One Retinoblastoma World Map. <https://map.1rbw.org/> (accessed April-November 2021)

Stacey AW et al. (2021) Incidence of retinoblastoma has increased: results from 40 European countries. Ophthalmology 128:1369-71

## TREATMENT

Abramson DH et al. (2015) Advanced unilateral retinoblastoma: the impact of ophthalmic artery chemosurgery on enucleation rate and patient survival at MSKCC. PLoS ONE 10:e0145436

Ancona-Lezama D et al. (2020) Modern treatment of retinoblastoma: a 2020 review. Indian J Ophthalmol 68:2356-65

Tomar AS et al. (2021) Global retinoblastoma treatment outcomes. Association with national income level. 128:740-53

# OV COMPANY REFERENCES

## **CG Oncology CG0070 (cretostimogene grenadenorepvec)**

<https://cgoncology.com>

Ramesh N et al. (2006) CG0070, a conditionally replicating granulocyte macrophage colony-stimulating factor-armed oncolytic adenovirus for the treatment of bladder cancer. Clin Cancer Res 12:305

Svatek RS et al. (2024) PIVOT-006: A Phase 3, Randomized Study of cretostimogene grenadenorepvec versus Observation for the Treatment of Intermediate Risk NMIBC Following TURBT. Abstract TPS715. Presentation at ASCO Genitourinary Symposium 2024. J Clin Oncol 42:TPS715

Tyson M et al. (2023) First Results from BOND-003: Phase 3 study of cretostimogene grenadenorepvec Monotherapy for Patients with BCG Unresponsive High-Risk NMIBC with CIS +/-Papillary (Ta/T1) Tumors. Presentation at Society of Urologic Oncology Annual Meeting SUO 2023.

Uchio EM et al. A phase 3, single-arm study of CG0070 in subjects with non-muscle invasive bladder cancer (NMIBC) unresponsive to Bacillus Calmette-Guerin (BCG). J Clin Oncol 40:TPS598

## **Genelux Corporation Olvi-Vec (GL-ONC1, GLV-1h68, olvimulogene nanivacirepvec)**

<https://genelux.com>

Clinicaltrials.gov NCT05281471: Efficacy & safety of Olvi-Vec and platinum-doublet + bevacizumab compared to platinum-doublet + bevacizumab in platinum-resistant/refractory ovarian cancer (OnPrime, GOG-3076)

Holloway RW et al. (2023) Clinical activity of olvimulogene nanivacirepvec–primed immunochemotherapy in heavily pretreated Patients With Platinum-Resistant or Platinum-Refractory Ovarian Cancer. The Nonrandomized Phase 2 VIRO-15 Clinical Trial. JAMA Oncol. 9:903

Lin D et al. (2023) Oncolytic virotherapy: basic principles, recent advances and future directions. Signal Transduct Target Ther. 8:156

Mell LK et al. (2017) Phase I trial of Intravenous oncolytic vaccinia virus (GL-ONC1) with cisplatin and radiotherapy in patients with locoregionally advanced head and neck carcinoma. Clin Cancer Res 23:5696

Zhang Q et al. (2007) Eradication of solid human breast tumors in nude mice with an intravenously injected light-emitting oncolytic vaccinia virus. Cancer Res 67:10038

# OV COMPANY REFERENCES

## **Oncolytics Biotech: Pelareorep (formerly Reolysin®)**

<https://oncolyticsbiotech.com>

Arnold D et al. Pelareorep (pela) + atezolizumab (atezo) and chemotherapy in first-line (1L) advanced or metastatic pancreatic ductal adenocarcinoma (PDAC) patients – Results from the GOBLET study. Poster presentation at the European Society for Molecular Oncology Annual Congress ESMO 2023.

Clements D et al. (2014) Reovirus in cancer therapy: an evidence-based review. *Oncolytic Virother* 3:69

Lin D et al. (2023) Oncolytic virotherapy: basic principles, recent advances and future directions. *Signal Transduct Target Ther.* 8:156

Philips MB et al. (2018) Current understanding of reovirus oncolysis mechanisms *Oncolytic Virother* 7:53

Xie R et al. (2023) Effectiveness and safety of pelareorep plus chemotherapy versus chemotherapy alone for advanced solid tumors: a meta-analysis. *Front Pharmacol* 14:1228225

## **Replimune: RP1,RP2 (vusolimogene oderparepvec)**

<https://replimune.com>

Chmielowski et al. (2023) Initial efficacy and safety of RP1 + nivolumab in patients with anti-PD1–failed melanoma from the ongoing phase 1/2 IGNYTE study. Abstract 9609. Poster presentation American Society of Clinical Oncologists Annual Meeting ASCO 2023. *J Clin Oncol* 41:9509

Sacco JJ et al. (2023) Preliminary safety and efficacy results from an open-label, multicenter, phase 1 study of RP2 as a single agent and in combination with nivolumab in a cohort of patients with uveal melanoma. Presentation at the International Congress of the Society for Melanoma Research SMR 2023.

Thomas S et al. (2019) Development of a new fusion-enhanced oncolytic immunotherapy platform based on herpes simplex virus type 1. *J ImmunoTher Cancer* 7:214