Unique Oncolytic Virus Therapies for Multiple Solid Tumors

January 2026

Theriva BIOLOGICS

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 oncolytic viruses (OVs) being promising cancer therapeutics; the multiple potential value opportunities for VCN-01; the regulatory status expected to facilitate VCN-01 development; potential access to a priority review voucher; the therapeutic potential of VCN-01 and other Theriva OVs; the ability of VCN-01 and other Theriva OVs to overcome key OV challenges; the potential of VCN-01 to enable immuno-oncology therapies in refractory tumors; the clinical advancement of VCN-01 and other Theriva OVs in diverse cancer indications (including pancreatic ductal adenocarcinoma, head and neck cancer, ovarian cancer, colorectal cancer, and retinoblastoma) and the projected milestones. Important factors that could cause actual results to differ materially from current expectations include, among others, the Company's ability to enroll patients as planned and reach clinical trial milestones when anticipated; the Company's ability to complete clinical trials on time and achieve the desired results and benefits; the Company's product candidates demonstrating safety and effectiveness, including positive clinical data that demonstrates VCN-01 may lead to improved clinical outcomes for patients; 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 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 products; developments by competitors that render such products obsolete or non-competitive; the Company's ability to maintain license agreements; the continued maintenance and growth of the Company's patent estate; the ability to continue to remain well financed; 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

- VCN-01 lead candidate undergoing Phase 3 clinical trial preparation[1]
  - First-line metastatic pancreatic cancer
  - Retinoblastoma (rare pediatric disease)
- VCN-01 Phase 1 clinical data support potential in additional indications[2]
- VCN-X innovative discovery engine developing a distinct product pipeline of oncolytic viruses
- Seeking financing and/or partnerships to execute planned pivotal trial programs

Financial Snapshot	
Exchange	NYSE American
Ticker	TOVX
Cash (10Nov2025)	$15.5M
Projected cash runway	Q1 2027
Average Daily Volume (3M)	18.75M[3]
Locations	Rockville, MD Barcelona, Spain

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[1]In combination with standard-of-care chemotherapy. [2]Colorectal cancer, head-and neck squamous cell carcinoma; combinations with immune checkpoint inhibitors, CAR-T cells. [3]At 10Jan2026 Yahoo! Finance

VCN-01 IS A UNIQUELY ENGINEERED HUMAN ADENOVIRUS 5

Designed to have multiple anti-tumor actions

Systemic

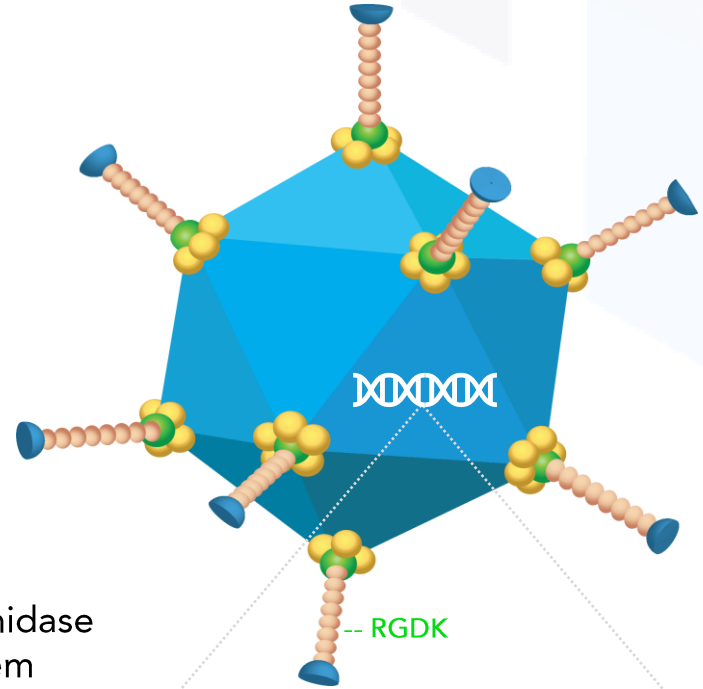
VCN-01 targets both primary and metastatic lesions

Selective

Virus replicates only in tumor cells
Liver detargeted

Stroma Degrading

Replicating virus expresses PH20 hyaluronidase
Exposes solid tumors to the immune system
and diverse co-administered therapies



E2F binding +++ → E1a-Δ24 → MLP → PH20

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Replication enhanced by significantly increased E2F binding. E1a-Δ24 gene deletion means replication only in cells with a defective Rb-E2F pathway.
Fiber shaft RGDK modification. PH20 soluble human testicular hyaluronidase enzyme expression is under control of the virus major late promoter (MLP).

THERIVA PIPELINE

Candidate	Target	Pre-IND	Phase 1	Phase 2	Phase 3	Sites	Status*
VCN-01 Selective, Stroma Degrading OV	Pancreatic Cancer (IV) with gemcitabine/nab-paclitaxel					Multicenter Spain, USA	**Preparing Phase 3** Orphan Drug Designation US, EU Fast Track Designation US
	Retinoblastoma (IVit)					Sant Joan de Déu Hospital Materno-Infantil Universitat de Barcelona	**Planning Phase 2/3** Orphan Drug Designation US, EU Rare Pediatric Disease Designation US
	HNSCC (IV) + durvalumab					ICO Institut Català d'Oncologia	**Phase 1 Complete**
	Brain tumors (IV)					LEEDS	**Phase 1 On-going**
VCN-X and Albumin Shield OVs	Solid tumors (IV)					ICO Institut Català d'O; IDIBELL	**Preclinical Studies On-going**
SYN-004 [1] Oral β-lactamase	**Prevention of aGVHD in allo-HCT**					Washington University in St. Louis	**Phase 1b/2a On-going**
SYN-020[2] Oral IAP	**Multiple potential GI and metabolic indications**						**Phase 1 Studies Complete**

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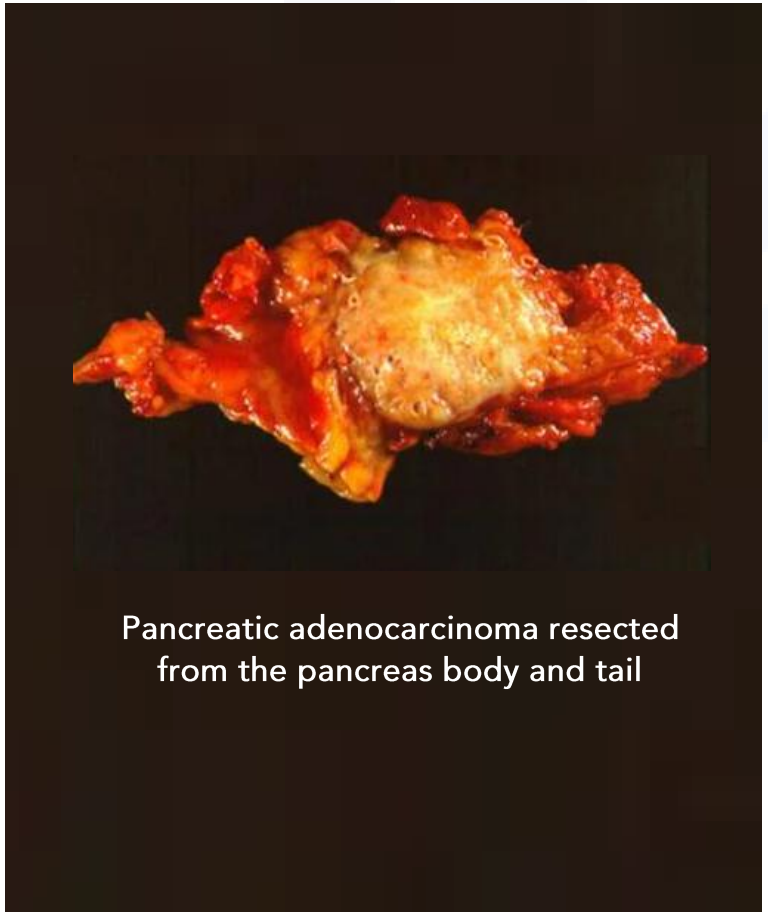
*Based on Management's current beliefs and expectations. aGVHD acute graft-vs-host disease; allo-HCT allogeneic hematopoietic cell transplant. HNSCC head and neck squamous cell carcinoma. IV intravenous. IVit intravitreal. ¹Final Phase 1b/2a study cohort contingent on grant funding or partnership. ²Pursuing out-licensing.

VCN-01 LEAD INDICATION PANCREATIC CANCER

Highly fatal cancer protected by dense tumor stroma

- Orphan disease, highest mortality of all solid tumors
  - Median survival 8-11 months for metastatic disease[1,2]
  - USA est. 67,440 new cases and 51,980 deaths in 2025[3]
- Hyaluronic acid in stroma is associated with reduced treatment efficacy and poor prognosis[4]
  - VCN-01 designed to degrade hyaluronic acid
- Incidence is growing worldwide
  - Est. treatment market ~$2.9B (2024) ~$6.0B (2030)[5]



Pancreatic adenocarcinoma resected from the pancreas body and tail

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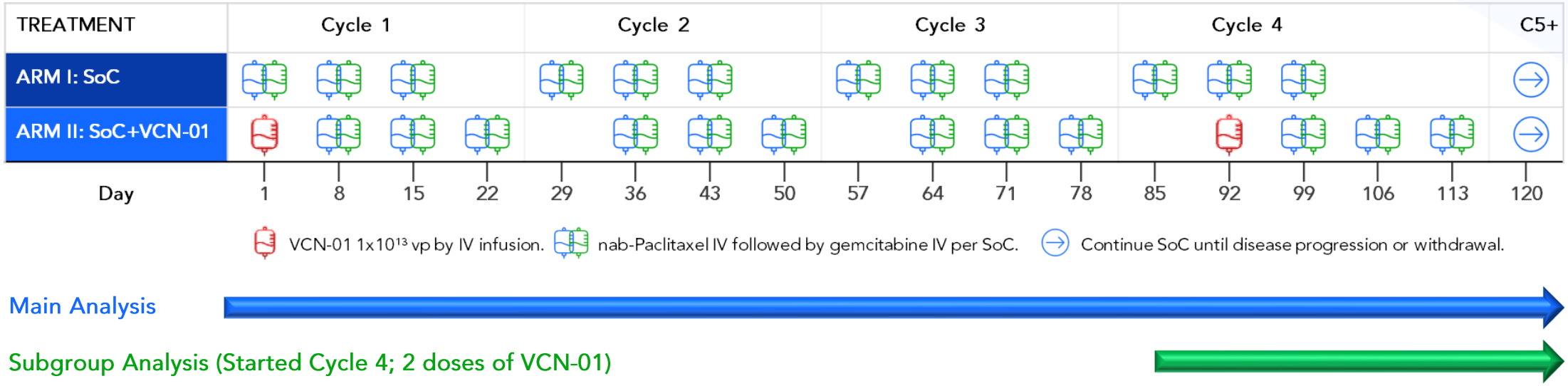
[1]Michael (2019) BMC Palliat Care 18:13, Bengtsson (2020) Sci Rep 10:16425, Carioli (2021) Ann Oncol 32:478, ASCO Pancreatic Cancer Statistics. [2]SEER Cancer Stat Facts: Pancreatic Cancer website. [3]American Cancer Society. Cancer Facts & Figures 2025. Atlanta: American Cancer Society; 2025. [4]Tahkola (2021) Sci Rep 11:12216, Placencio-Hickok (2022) Pancreatology 22:92. [5]Grand View Research website.

VIRAGE PANCREATIC CANCER PHASE 2B CLINICAL TRIAL

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

- Patients with newly-diagnosed metastatic pancreatic ductal adenocarcinoma (first line)
- Primary endpoints overall survival, VCN-01 AE profile and tolerability
- Secondary endpoints included progression free survival, duration of response



Study designed with 80% power to detect a hazard ratio (HR) of 0.51-0.65 for OS with a 1-sided alpha of 0.05 (2-sided alpha 0.1). P-values are for 2-sided statistical analysis using the log rank test.

VIRAGE PHASE 2B TRIAL KEY FINDINGS

Data provide strong support for Phase 3 trial

- Enrolled a "real world" population of older and more fragile patients
- Increased overall and progression free survival (OS, PFS) and duration of response (DoR) observed in VCN-01 plus gemcitabine/nab-paclitaxel SoC treatment group compared to SoC alone
  - Additional survival benefit observed in patients receiving two doses VCN-01
  - Greater improvements at later timepoints consistent with immune MOA
- Acceptable AE profile consistent with prior VCN-01 clinical trials
- Better hazard ratios for OS, PFS, DoR vs gemcitabine/nab-paclitaxel than reported in NALIRIFOX Phase 3 trial[1]

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[1]Wainberg (2023) Lancet 402:1272. NALIRIFOX leucovorin+ 5-FU+liposomal irinotecan+oxaliplatin.

VIRAGE DEMOGRAPHICS

Parameter	Statistics	Main Analysis (FAS)[1]		Subgroup Analysis (Two Doses VCN-01)[2]	
		SoC	VCN-01 + SoC	SoC C4+	2*VCN-01 + SoC
No. Patients (% of cohort)	n (%)	48	48	29 (60.4)	34 (70.8)
Age (years)	Mean (SD)	69.5 (8.25)	66.0 (8.97)	68.1 (8.31)	65.8 (9.71)
	Median	68.5	66.0	66.0	66.0
<65 yrs	n (%)	10 (20.8)	18 (37.5)	8 (27.6)	13 (38.2)
≥65 yrs	n (%)	38 (79.2)	30 (62.5)	21 (72.4)	21 (61.8)
Gender					
Male	n (%)	22 (45.8)	23 (47.9)	13 (44.8)	17 (50.0)
Female	n (%)	26 (54.2)	25 (52.1)	16 (55.2)	17 (50.0)
ECOG at randomization					
0	n (%)	17 (35.4)	19 (39.6)	14 (48.3)	15 (44.1)
1	n (%)	31 (64.6)	29 (60.4)	15 (51.7)	19 (55.9)
ECOG at Cycle 4					
0	n (%)	..	..	6 (20.7)	14 (41.2)
1	n (%)	..	..	23 (79.3)	19 (55.9)
2	n (%)	..	..	..	1 (2.9)

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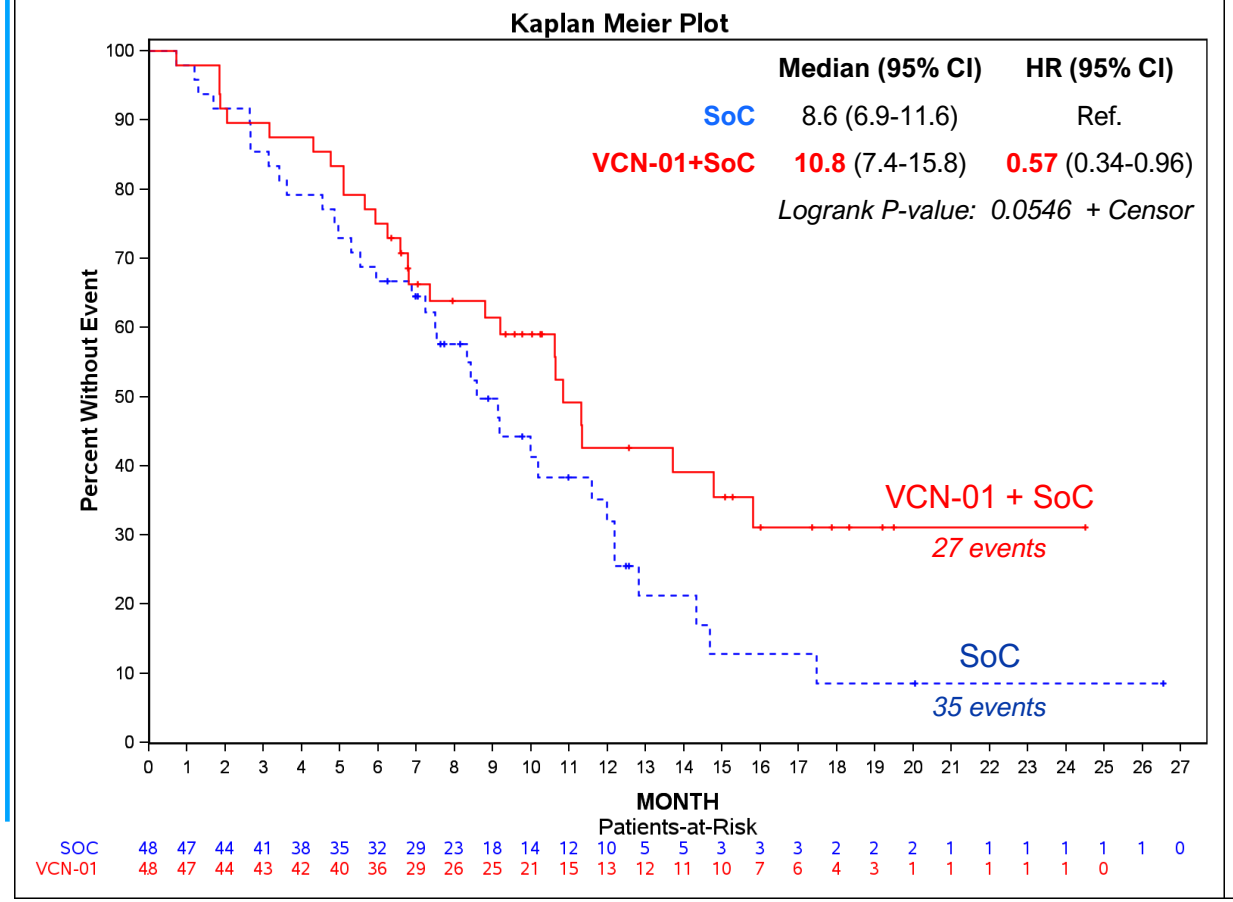
[1]Full Analysis Set (FAS) patients received at least 1 dose of gemcitabine/nab-paclitaxel (SoC) in each arm.
[2]Compares patients in ARM II who received a second dose of VCN-01 followed 1-week later by cycle 4 of SoC to patients in ARM I who started cycle 4 of SoC (C4+). *These patients were not preselected for inclusion in subgroup analysis; anyone who reached cycle 4 was included.*

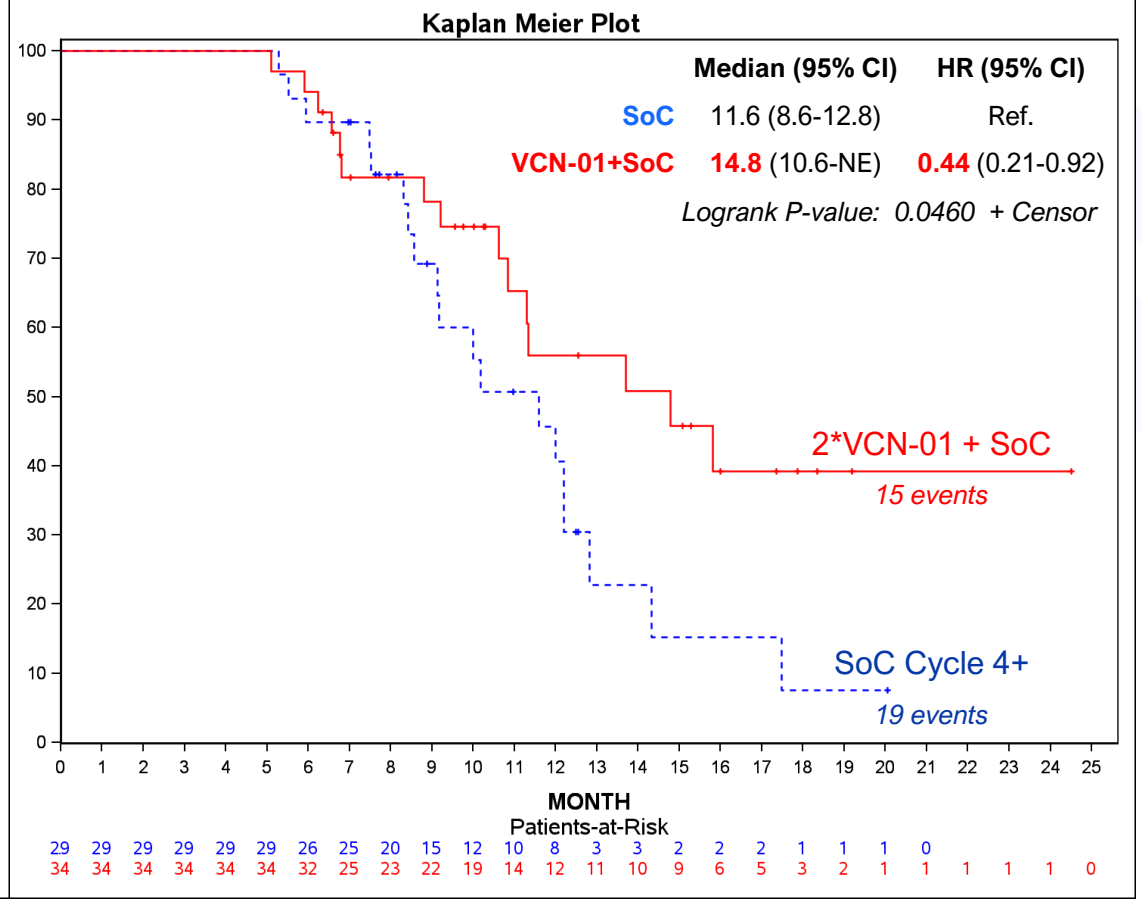
INCREASED OVERALL SURVIVAL IN VCN-01+SOC ARM

Greater OS improvement with two VCN-01 doses

Main Analysis Population[1]



Two doses of VCN-01[2]

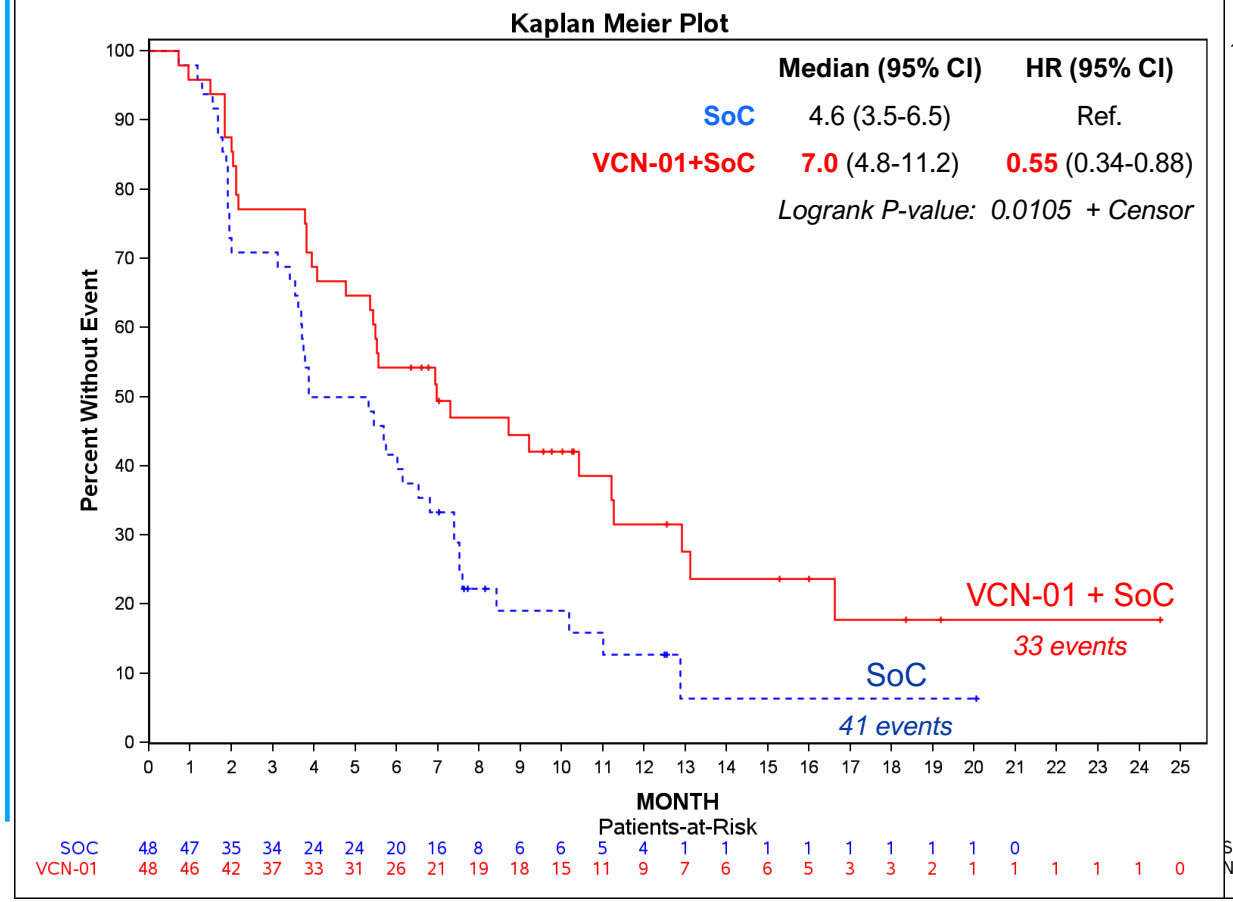


[1]Full Analysis Set (FAS) compares patients who received at least 1 dose of gemcitabine/nab-paclitaxel (SoC) in each arm.
[2]Compares patients in ARM II who received a second dose of VCN-01 followed 1-week later by cycle 4 of SoC to patients in ARM I who started cycle 4 of SoC. 70.8% of patients in the VCN-01+SoC arm received 2 doses of VCN-01.

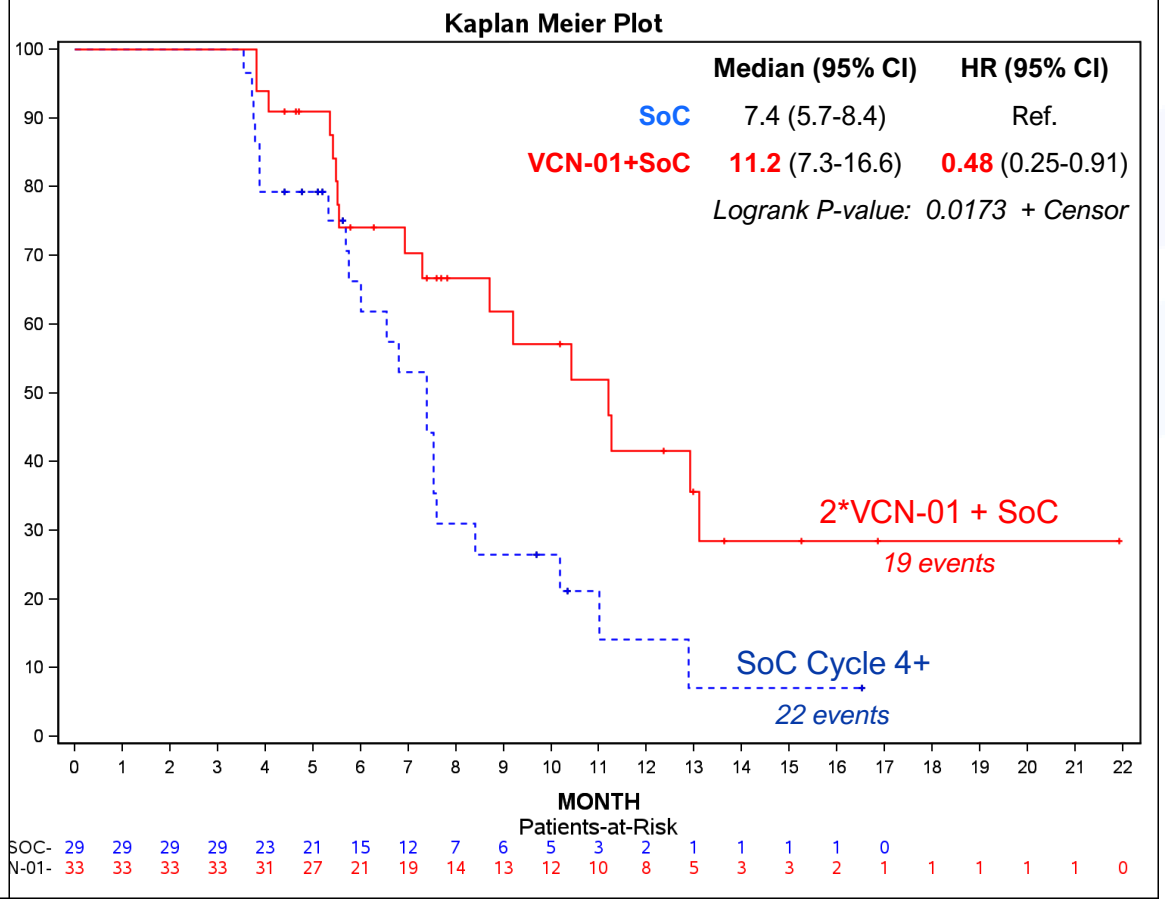
INCREASED PROGRESSION-FREE SURVIVAL IN VCN-01+SOC ARM

Greater PFS improvement with two VCN-01 doses

Main Analysis Population[1]



Two doses of VCN-01[2]

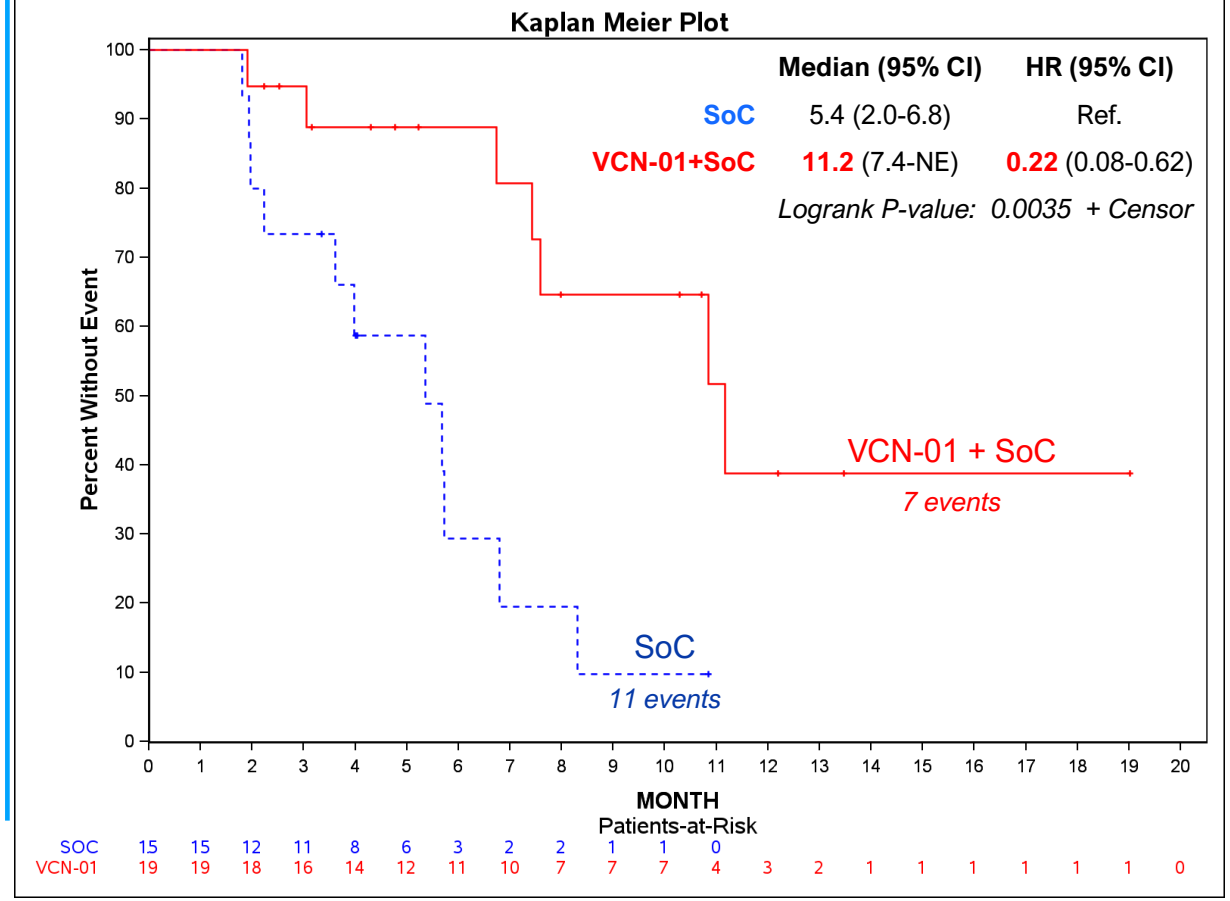


[1]Full Analysis Set (FAS) compares patients who received at least 1 dose of gemcitabine/nab-paclitaxel (SoC) in each arm.
[2]Compares patients in ARM II who received a second dose of VCN-01 followed 1-week later by the cycle 4 of SoC to patients in ARM I who started cycle 4 of SoC. 70.8% of patients in the VCN-01+SoC arm received 2 doses of VCN-01.

DURATION OF RESPONSE DOUBLED IN VCN-01+SOC ARM

Increased response rate with two VCN-01 doses

Patients who had a Partial or Complete Response[1]



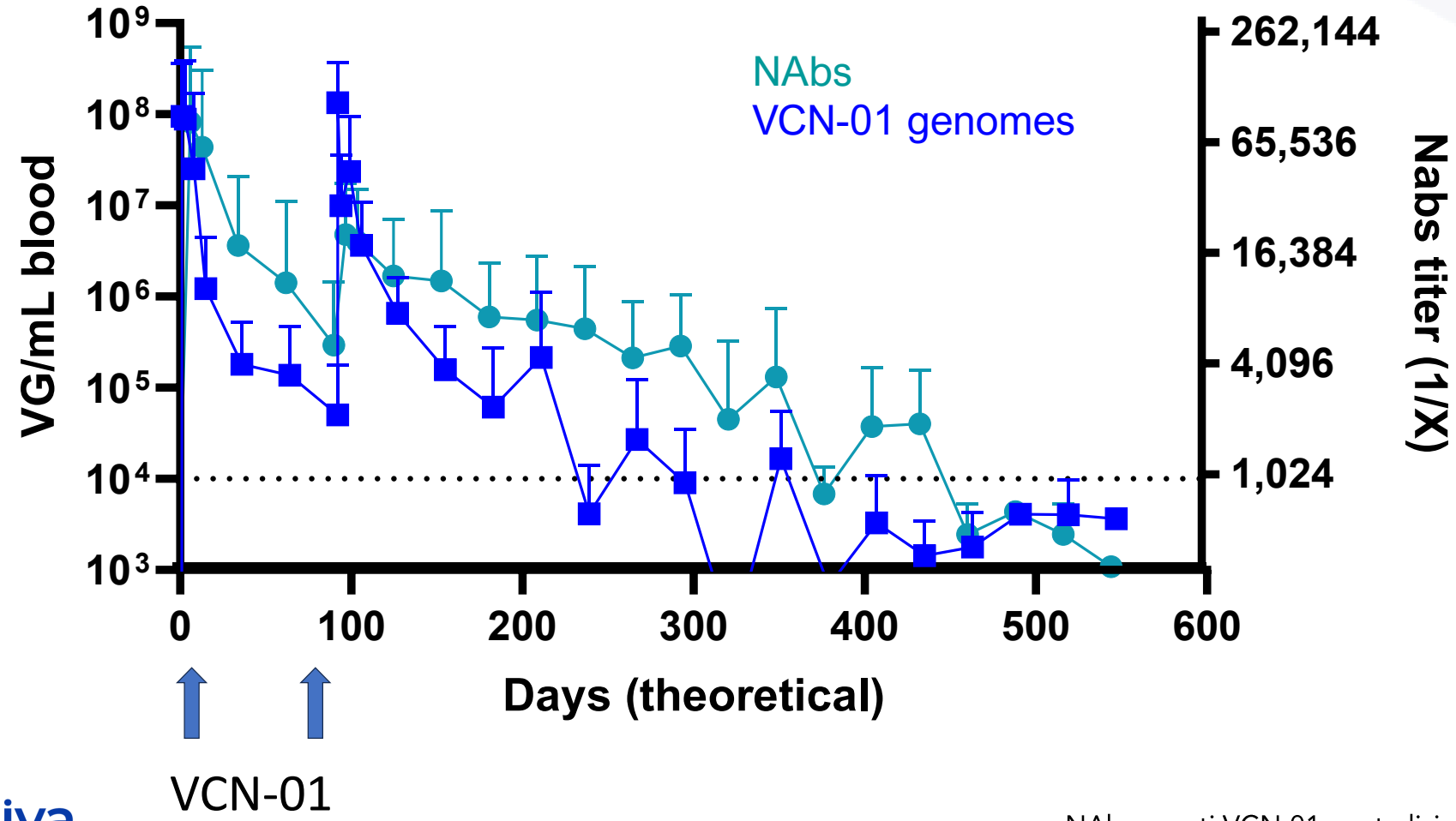
Objective Response Rates (ORR)[1]

	Main Analysis (FAS)[1]		Subgroup (2 Doses VCN-01)[2]	
N (%)	**SoC**	**VCN-01 + SoC**	**SoC C4+**	**2*VCN-01 + SoC**
Patients	48	48	29	34
CR	0	1	0	1
PR	15	18	14	18
ORR	15 (31.3%)	19 (39.6)	14 (48.3%)	19 (55.9%)
		p=0.314		*p=0.533*

[1]According to RECIST 1.1 using CT scan evaluations by sites. Data are for the Full Analysis Set (FAS) which comprises patients who received at least 1 dose of gemcitabine/nab-paclitaxel (SoC) chemotherapy in each arm. CR complete response, PR partial response.

VIRAGE BIOLOGICAL DATA SUPPORT REPEAT DOSING

Circulating viral genomes and NAbs similar after both VCN-01 doses

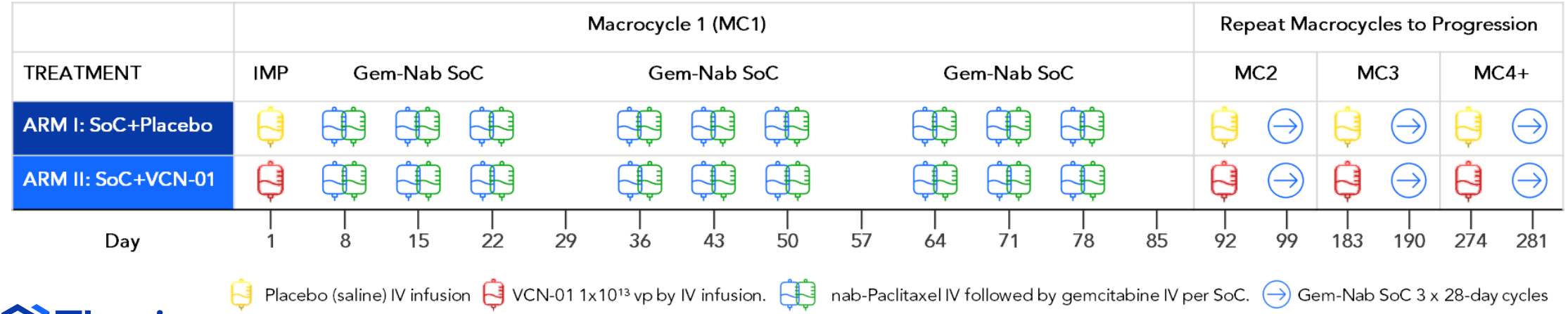


NAbs = anti-VCN-01 neutralizing antibodies

PROPOSED PHASE 3 TRIAL IN PANCREATIC CANCER

Repeated VCN-01 dosing intended to improve outcomes

- Patients with newly-diagnosed metastatic pancreatic ductal adenocarcinoma (first line)
- Multicenter, double-blinded, placebo-controlled, randomized (1:1), controlled trial
- Repeated 3-month "macrocycles" comprising 1 IV dose of VCN-01 ($1x10^{13}$ vp) or placebo administered 7-days prior to 3 x 28-day cycles of gemcitabine/nab-paclitaxel SoC
- Primary endpoint: overall survival
- Adaptive design with an initial sample size of ~450 patients



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PURSUING REGULATORY AGREEMENT ON PHASE 3 DESIGN

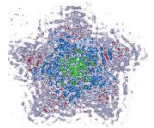
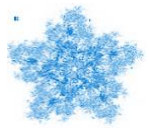
- Positive Scientific Advice from European Medicines Agency (EMA)
  - Agreed on proposed inclusion/exclusion criteria, primary endpoint (OS), and secondary endpoints (including PFS, DoR, and patient reported outcomes)
  - Agreed on proposed sample size and adaptive trial design with two interim analyses
  - Agreed that a single study, if successful, could support a marketing authorization
  - Recognized the survival benefit of the second VCN-01 dose in the VIRAGE trial; suggested potentially more frequent dosing
  - Requested additional VCN-01 genome and anti-VCN-01 Ab measurements for the additional doses
- FDA End-of-Phase 2 Meeting Requested
  - Meeting to review proposed Phase 3 trial design anticipated Q1 2026

VCN-01 ADDITIONAL CLINICAL ACTIVITIES

- Potential Phase 1b study in PDAC to explore more frequent VCN-01 dosing (q2 months) to potentially improve outcomes
  - Builds on EMA suggestion and recognition of the benefit of multiple VCN-01 doses
  - VCN-01 dosing q2 months means at least two doses could be administered to most patients (PFS 3.5-6.5 months in VIRAGE study)
  - Small study (n=6-10) could be conducted with existing cash and available clinical drug product
- Planning a potential pivotal trial in retinoblastoma (Rb)
  - Intravitreal VCN-01 plus topotecan in children with refractory vitreous seeds
  - Extremely rare pediatric disease may permit a relatively small, single-arm study
  - Rare Pediatric Disease designation may enable access to monetizable Priority Review Voucher
  - No prior approvals in Rb, pursuing close collaboration with regulators

THERIVA OV PIPELINE DISCOVERY AND DEVELOPMENT

Advancing founders' decades of world leading OV innovation

Common Features	Product Specific Features
Clinically-tested Adenovirus Expressing PH20 Hyaluronidase to Degrade Tumor Stroma	 VCN-01 Hyaluronidase alone
+	
Additional Transgene Payloads to Enhance Anti-tumor Immune Response and Potentially Enable Single-Agent therapy	 VCN-12 Hyaluronidase + Toxins
+ / -	
Albumin Shield™ To Prevent Neutralization by Anti-viral Antibodies and Facilitate IV Multidosing	 VCN-11 Hyaluronidase + Albumin Shield

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2026 PROJECTED MILESTONES

VCN-01 FDA EOP2
Phase 3 study design

VIRAGE AACR Presentation
Abstract submitted

VCN-01 PDAC Phase 1
More frequent dosing, PK/PD

VCN-01 PDAC Phase 3
If funding obtained

VCN-01 Rb FDA Meeting
Review Ph 2-3 study design

Potential Out-license of Legacy Asset

VCN-12 candidate
*Next generation OV**

VCN-01 CMC Scale-up
If funding obtained

SYN-004 in allo-HCT
Initiate final Phase1b/2a cohort‡

Partnering and Strategic Activities

Q1 2026	Q2 2026	Q3 2026	Q4 2026

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*VCN-12 is an armed derivative of VCN-01 designed to express an additional functional payload. Allo-HCT allogeneic hematopoietic cell transplant.
‡Contingent on investigator grant funding. AACR American Association for Cancer Research Annual Meeting 17-22Apr2026, San Diego CA. EOP2 End of Phase 2 meeting with FDA. Rb retinoblastoma.

APPENDIX

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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

Manel Cascalló PhD

General Director, EU Subsidiary

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

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

VCN BIOSCIENCES

Vince Wacher 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

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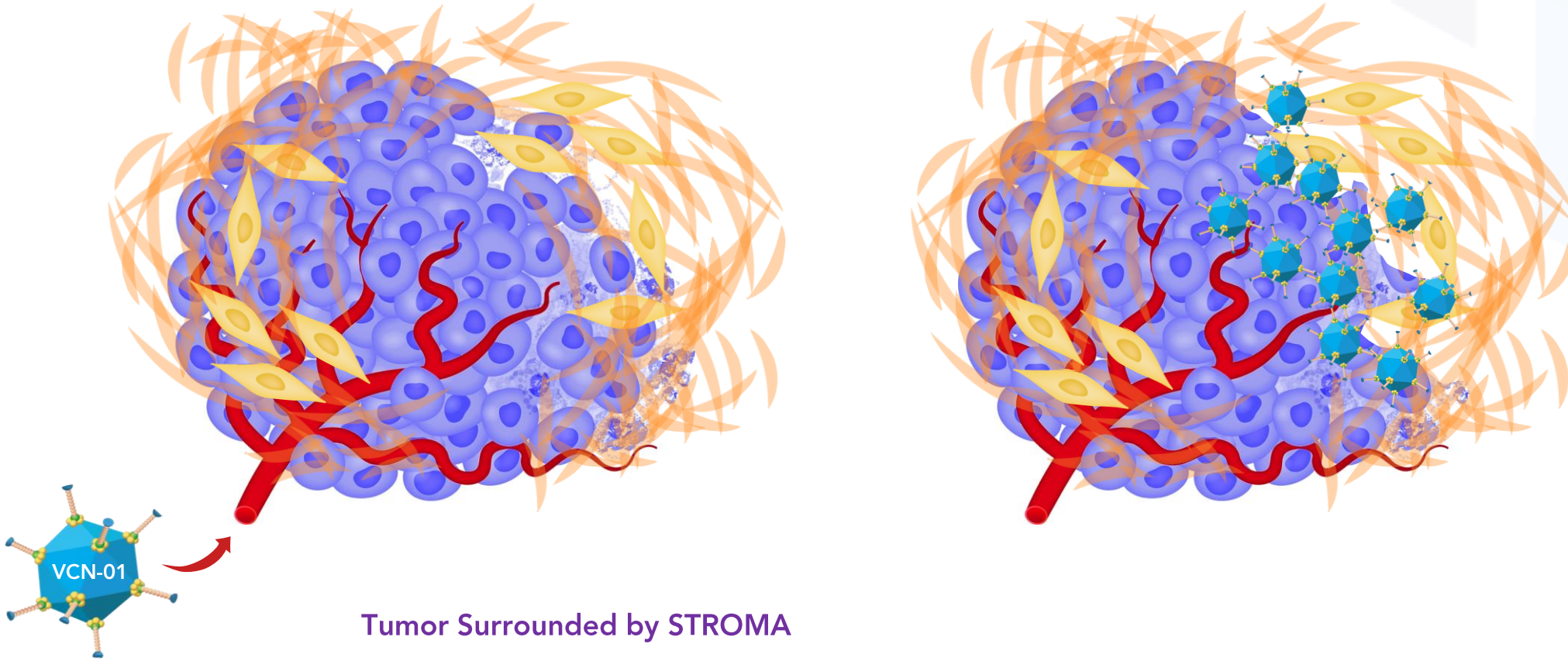
VCN-01 IS A UNIQUELY ENGINEERED HUMAN ADENOVIRUS 5

1 SYSTEMIC delivers VCN-01 to the primary tumor and metastases and detargets the liver

2 SELECTIVE replication at very high levels lyses tumor cells directly without harming healthy tissues



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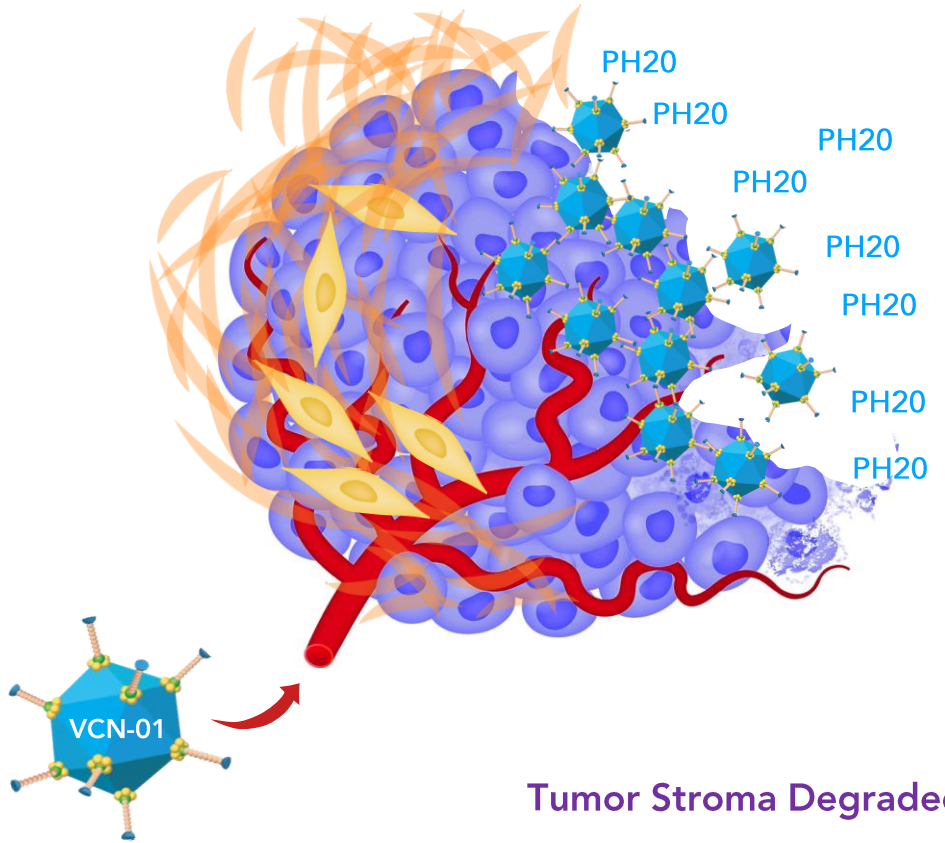
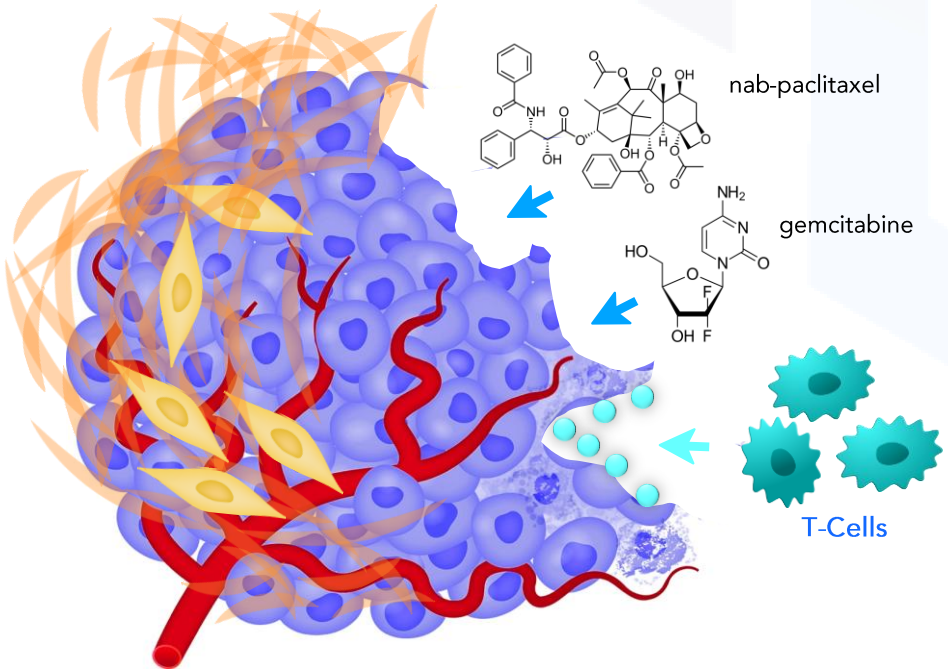
VCN-01 DESIGNED TO HAVE MULTIPLE ANTI-TUMOR ACTIONS

3 STROMA degradation by PH20 facilitates solid 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



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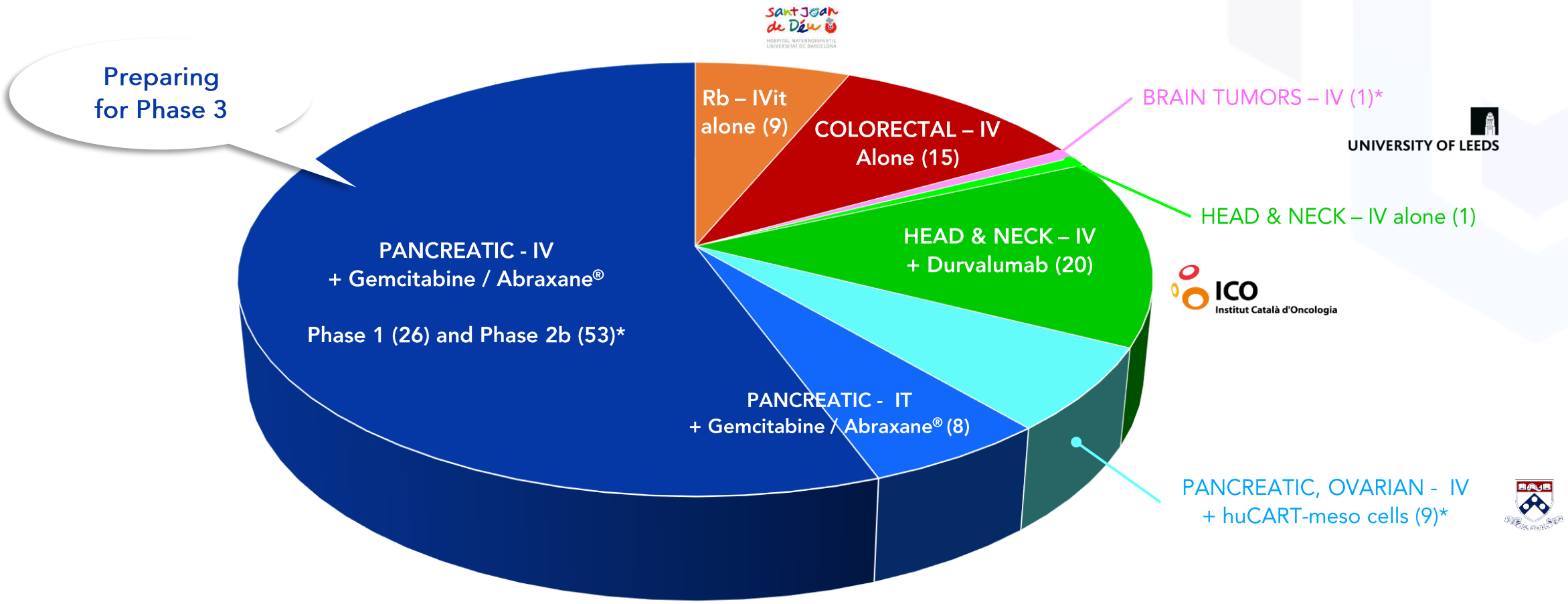
VCN-01 EXTENSIVE CLINICAL EXPERIENCE

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



(Number of VCN-01 Patients Treated in Parentheses)

*On-going study. Abraxane® - nab-paclitaxel. Durvalumab (IMFINZI®, AstraZeneca) is an anti-PD-L1 mAb immune checkpoint inhibitor. huCART-meso are autologous T cells engineered to express an extracellular single chain variable fragment (scFv) with mesothelin specificity. IT - intratumoral. IV - intravenous. IVit - intravitreal. Rb - retinoblastoma. See Appendix for study registry numbers and publications.

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[1]	$3.7M	$2.07B	$102.3M	$48.5M	$753.9M
Product	**VCN-01**	**Cretostimogene grenadenorepvec**	**Olvi-Vec**	**Pelareorep**	**RP1, RP2**
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	$1x10^{13}$ vp[2]	$1x10^{12}$ vp	$3x10^{9}$ pfu	$4.5x10^{10}$ $TCID_{50}$	$1x10^{7}$ pfu/mL
Stroma Degrading	Yes	No	No	No	No
Biomarker	PH20	..	β-GAL, β-GLU, GFP	..	..

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[1]At 30Apr2025 per *yahoo!* finance. [2]Approximately $7x10^{11}$ $TCID_{50}$. References describing the different OV product candidates are provided in the appendix; information is also available on each company's website and clinicaltrials.gov

THERIVA OV PORTFOLIO HIGHLIGHTS

Multiple modes of action, indications and combinations

- Highly differentiated OVs designed to have multiple antitumor effects
  - Systemic administration, selective tumor replication, stroma degradation
- Multiple potential value opportunities for lead asset VCN-01
  - Preparing Phase 3 trial with SoC in first-line metastatic PDAC; planning Phase 2/3 trial in retinoblastoma
  - Phase 1 data support additional indications (HNSCC, CRC) and 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

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CPI immune checkpoint inhibitor. CRC colorectal cancer. HNSCC head and neck squamous cell carcinoma. PDAC pancreatic ductal adenocarcinoma. SoC standard of care (gemcitabine + nab-paclitaxel in PDAC).

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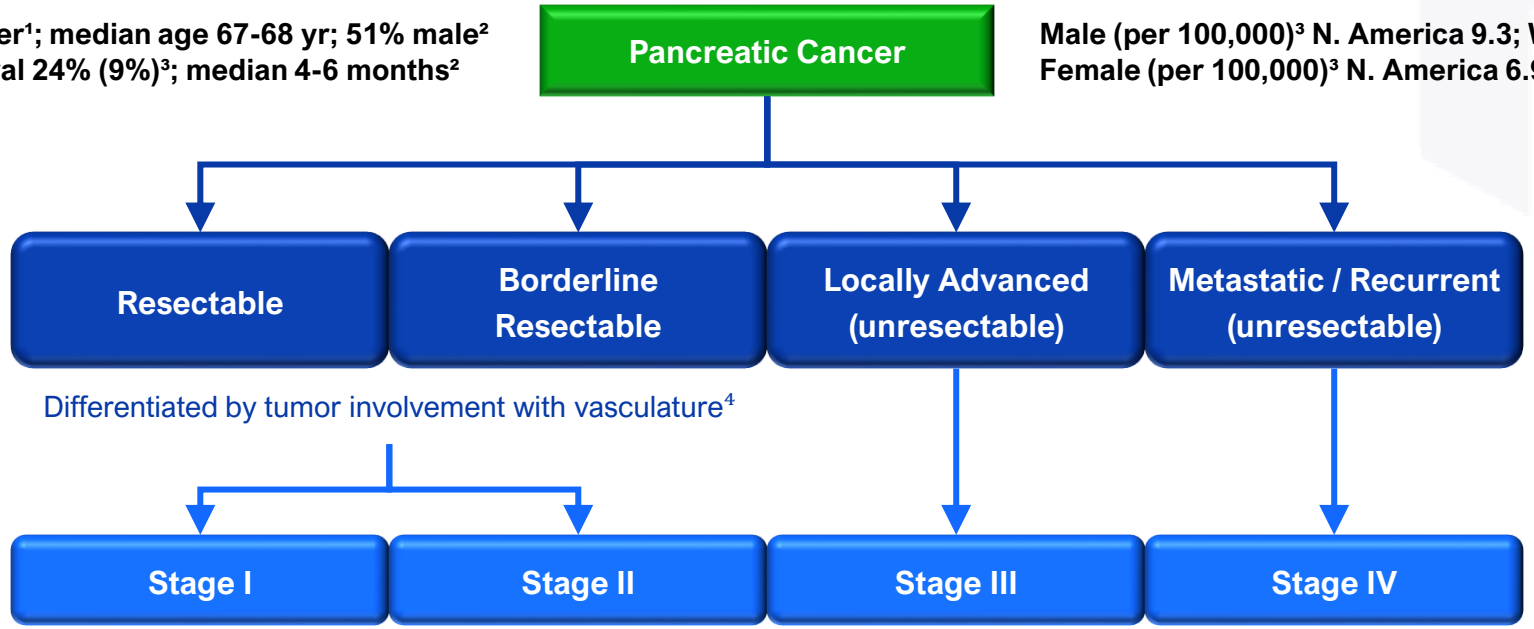
VCN-01 IN PANCREATIC CANCER

PANCREATIC CANCER STAGING

PDAC >90% pancreatic cancer[1]; median age 67-68 yr; 51% male[2]
1-year (5-year) overall survival 24% (9%)[3]; median 4-6 months[2]

Male (per 100,000)[3] N. America 9.3; W. Europe 9.9; E. Asia 7.0
Female (per 100,000)[3] N. America 6.9; W. Europe 7.4; E. Asia 4.8

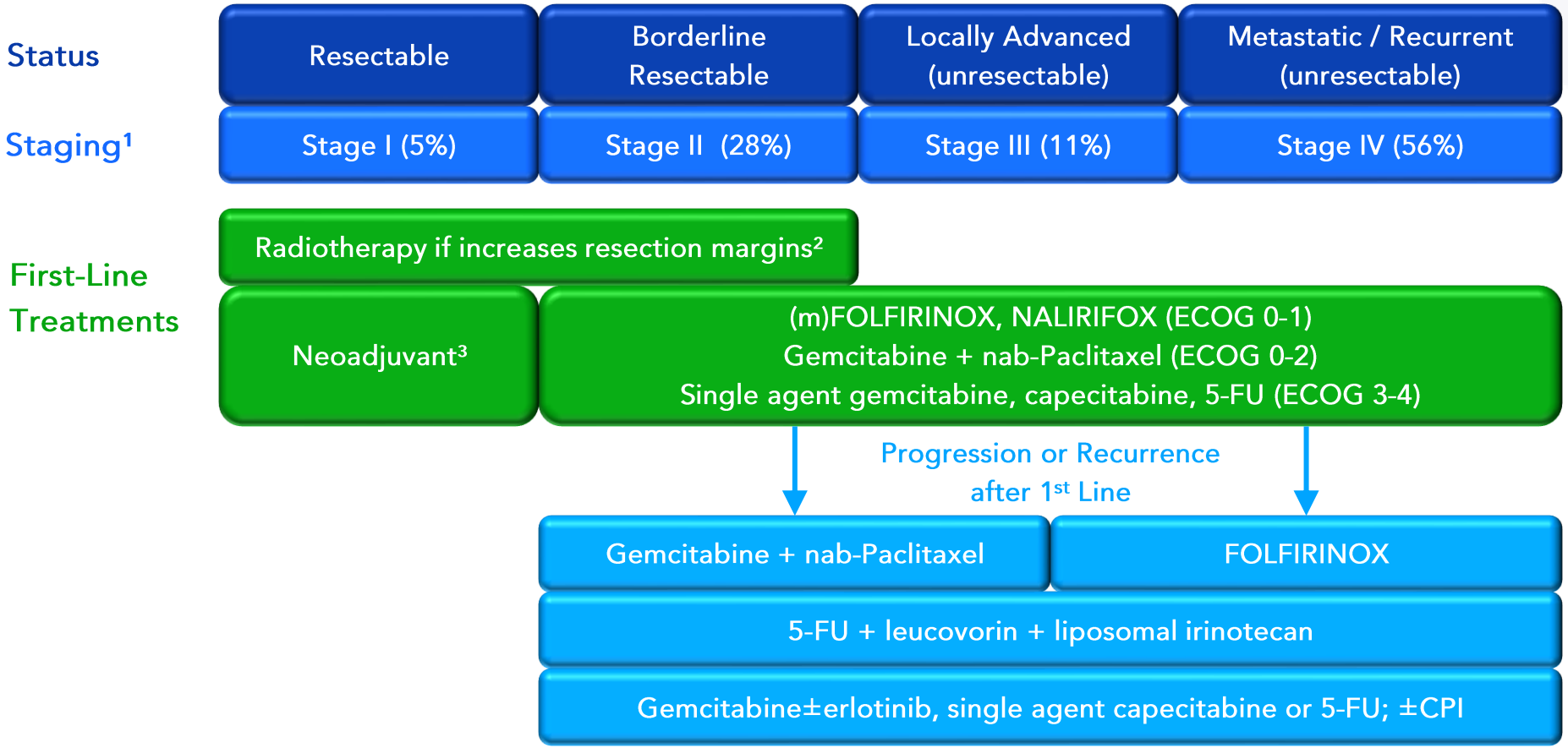


AJCC Stage	IA	IB	IIA	IIB	III	IV
T-N-M[5]	T1 N0 M0	T2 N0 M0	T3 N0 M0	T1-3 N1 M0	T1-3 N2 M0 T4 NX-2 M0	TX-4 NX-2 M1
Median Age, yr (range)[6]	66 (30-88)	66 (31-89)	68 (31-93)	66 (30-95)	67 (31-94)	67 (30-95)
Male (Female), %[6]	51 (49)	48 (52)	50 (50)	51 (49)	50 (50)	54 (46)
Proportion of PDAC, %[2]	1.3%	4.4%	11.5%	16.3%	10.6%	**56.0%**
5-Year Survival, %[2]	31.7%	11.8%	9.0%	8.7%	1.9%	**0.5%**
Pancreas Head, %[6]	61%	58%	77%	85%	75%	55%

Theriva BIOLOGICS

[1]**PDAC** pancreatic ductal adenocarcinoma. Cancers in the pancreas head (~70%) are diagnosed earlier than cancers in the body or tail (each ~15%), which have a worse prognosis, Sarantis (2020) *World J Gastrointest Oncol* **12:**173-181. [2]Bengtsson (2020) *Sci Rep* **10:**16425. [3]GLOBOCAN 2020 survey of persons 0-74 years. Ushio (2021) *Diagnostics* **11:**562. [4]Toesca (2018) *Int J Radiation Oncol Biol Phys* **100:**1155-1174. [5]American Joint Committee on Cancer **T**umor size, **N**odal involvement, **M**etastasis. [6]Yu (2015) *Gut* **64:**1783-9.

PANCREATIC CANCER CURRENT TREATMENTS



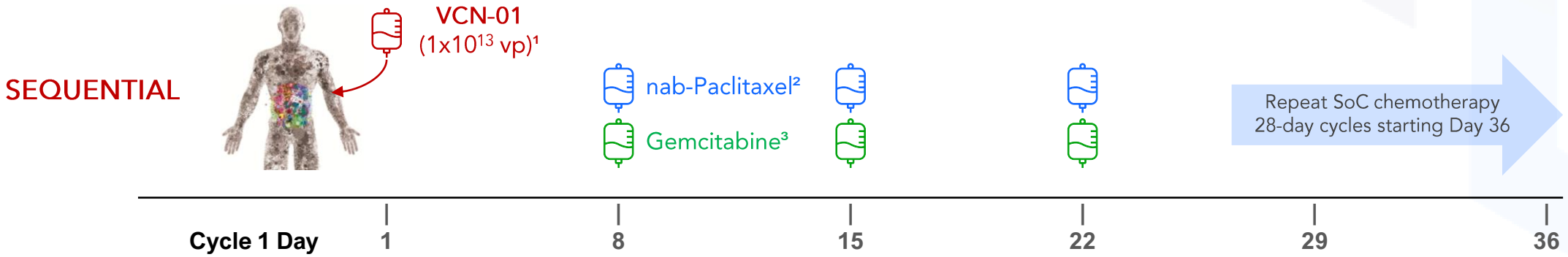
Additional treatments are available for small subsets of patients with gene mutations such as gBRCAm , NRG1 fusion

Theriva BIOLOGICS

[1]Bengtsson (2020) *Sci Rep* **10:**16425. [2]Used in <20% of PDAC cases. [3]Identical to first-line chemotherapy. CPI checkpoint inhibitor for cancers with microsatellite instability or deficient mismatch repair. ECOG Eastern Cooperative Oncology Group Performance Status. (m)FOLFIRINOX (modified) leucovorin+5-FU+irinotecan+oxaliplatin. nab-Paclitaxel nanoparticle albumin-bound paclitaxel. NALIRIFOX leucovorin+ 5-FU+liposomal irinotecan+oxaliplatin. Adapted from Tempero (2021) *J Natl Compr Canc Netw* **19:**439.

PREFERRED VCN-01 DOSING REGIMEN ESTABLISHED IN PHASE 1

Dose escalation in patients with metastatic pancreatic cancer



Encouraging clinical profile

Primary AEs fever, flu-like illness, reversible increase in liver enzymes

Survival and response rates better than published results for gemcitabine/nab-paclitaxel SoC

Clinical evidence of proposed MOA

VCN-01 viral genomes and increased immune markers detected in tumor biopsies

VCN-01 tumor penetration and replication indicated by persistent systemic PH20

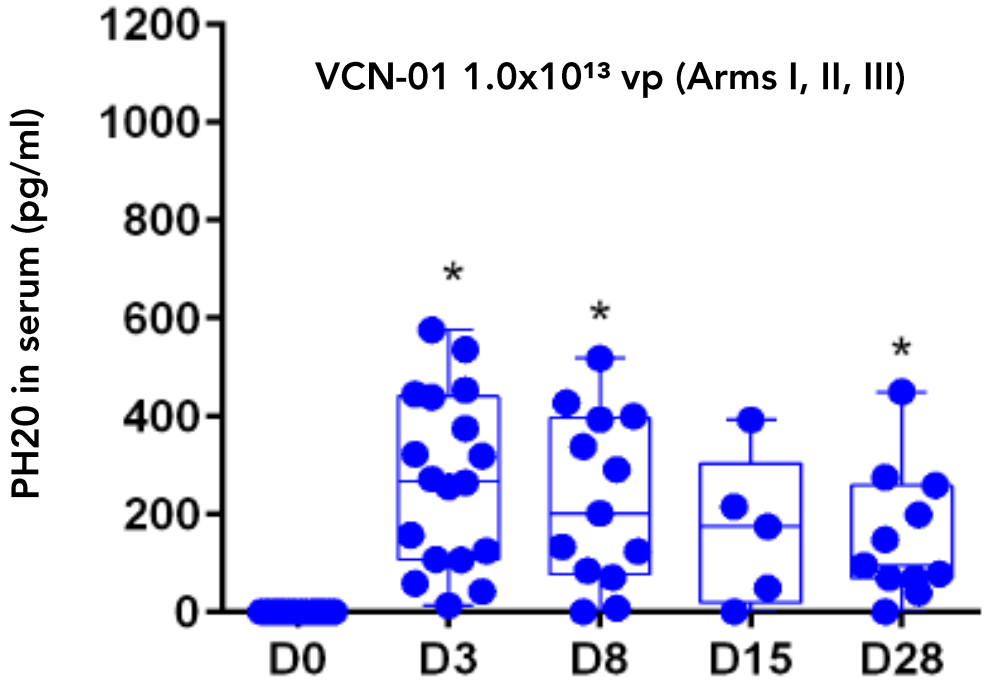
Theriva BIOLOGICS

[1]Single dose of VCN-01 administered by 10 min IV infusion. [2]nab-Paclitaxel (Abraxane®; 30 min infusion) administered at least 4 hours after VCN-01. [3]Gemcitabine (30 min infusion) administered immediately after Abraxane® infusion. Garcia-Carbonero (2022) J Immunother Cancer 10:e003255. [NCT02045602] SoC standard of care.

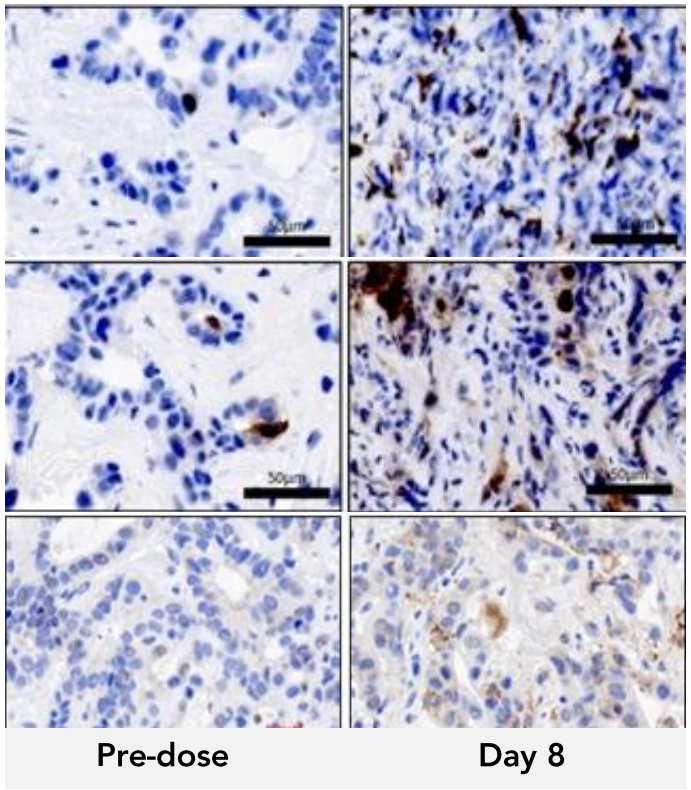
CLINICAL DATA SUPPORT VCN-01 MODE-OF-ACTION

Overcomes Neutralizing Antibodies and 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*



CD8⁺ lymphocytes

IDO upregulation

PD-L1 upregulation

*Data from VCN-01 Phase 1 Study, IDO indoleamine 2,3-dioxygenase, PD-L1 programmed death-ligand 1 and CD8⁺ lymphocyte infiltration measured by immunohistochemistry. PH20 (hyaluronidase) levels measured using an ELISA assay. Garcia-Carbonero (2022) J Immunother Cancer 10:e003255 [NCT02045602].

VIRAGE ENROLLMENT

Parameter	Spain	USA	Total
Sites Open	10	7	**17**
Screened	131	40	**171**
Screen Failure	42 (32%)	17 (43%)	**59 (35%)**
Randomized	89	23	**112**
SoC	44	11	**55**
VCN-01 + SoC	45	12	**57**
Treated*			
SoC	41	7	**48**
VCN-01 + SoC	39	9	**48**

Standard of care (SoC) is gemcitabine / nab-paclitaxel chemotherapy in repeated 28-day cycles
*Patients received at least one dose of SoC in each arm and comprise the Full Analysis Set
Five (5) additional patients received one dose of VCN-01 but no doses of SoC and are included in the Safety Population

Theriva BIOLOGICS

VIRAGE TREATMENT EMERGENT ADVERSE EVENTS

VCN-01 related events occurring in ≥5% of patients

Preferred Term – No. Patients (%)[a,b]	All Grades		Grade 3-4	
	First Dose (n=53)	Second Dose (n=36)	First Dose (n=53)	Second Dose (n=36)
Pyrexia	31 (58.5%)	19 (52.7%)	1 (1.9%)	-
Nausea	16 (30.2%)	6 (16.6%)	-	-
Asthenia	15 (28.3%)	4 (11.1%)	1 (1.9%)	1 (2.8%)
Vomiting	14 (26.4%)	9 (25.0%)	-	-
Aspartate aminotransferase increased	10 (18.9%)	1 (2.7%)	5 (9.4%)	-
Alanine aminotransferase increased	9 (16.9%)	1 (2.7%)	4 (7.5%)	-
Influenza like illness	9 (16.9%)	1 (2.7%)	7 (13.2%)	-
Transaminases increased	8 (15.1%)	2 (5.5%)	4 (7.5%)	-
Platelet count decreased/Thrombocytopenia	7 (13.2%)	1 (2.7%)	1 (1.9%)	-
Decreased appetite	7 (13.2%)	1 (2.7%)	-	-
Diarrhea	7 (13.2%)	3 (5.5%)	-	-
Fatigue	5 (9.4%)	-	-	-
Chills	5 (9.4%)	7 (19.4%)	-	-
Lymphocyte count decreased	4 (7.5%)	1 (2.7%)	3 (5.7%)	-
Gamma-glutamyl transferase increased	4 (5.7%)	-	3 (5.7%)	-
Anemia	3 (5.7%)	-	1 (1.9%)	-
Cytokine release syndrome	3 (5.7%)	2 (5.5%)	-	-

Additional Grade 3/4 AEs occurring <5%

Treatment-induced liver injury 2 (3.8%)
Neutrophil count decreased 1 (1.9%)
Lipase increased 1 (1.9%)
Alkaline phosphatase increased 1 (1.9%)
Neutropenia 1 (1.9%)
Hypotension 1 (1.9%)

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[a]Number of patients and [b]percentage of patients dosed presenting the treatment related adverse event (TEAE).
Note: events with a temporal continuity are accounted as only one with the highest grade

VIRAGE SAFETY REVIEW BY INDEPENDENT DMC

- VIRAGE clinical data was reviewed on two occasions by an independent Data Monitoring Committee (DMC) who noted the following:
  - Intravenous VCN-01 was well tolerated in patients treated in this study
  - The most common VCN-01 related AEs (pyrexia, flu-like illness, vomiting, nausea, and elevated transaminases) were transient and reversible.
  - AEs were observed to be less frequent and of reduced CTCAE grade after the second VCN-01 dose compared to the first VCN-01 dose
  - The overall type and number of AEs in the VCN-01+SoC treatment group was as expected for the pancreatic cancer population, the duration of treatment, and the administration of an oncolytic virus

VIRAGE COMPARED TO NALIFIROX NAPOLI 3

	Statistics	VIRAGE		NAPOLI 3[1]	
Treatment Arm		VCN-01+Gem/Nab	Gem/Nab	NALIRIFOX	Gem/Nab
Age (years)	n	48	48	383	387
	Median (range)	66.0 (41-86)	68.5 (52-85)	64 (20-85)	65 (36-82)
Sex					
Female	n (%)	25 (52.1)	26 (54.2)	179 (46.7)	157 (40.6)
Male	n (%)	23 (47.9)	22 (45.8)	204 (53.3)	230 (59.4)
ECOG					
0	n (%)	19 (39.6)	17 (35.4)	160 (41.8)	168 (43.4)
1	n (%)	29 (60.4)	31 (64.6)	222 (57.9)	219 (56.6)
OS (months)	Median [95% CI]	10.8 [7.4-15.8]	8.6 [6.9-11.6]	11.1 [10.0-12.1]	9.2 [8.3-10.6]
	HR [95% CI], p-value	**0.57** [0.34-0.96], 0.0546	..	**0.83** [0.70-0.99], 0.036	..
PFS (months)	Median [95% CI]	7.0 [4.8-11.2]	4.6 [3.5-6.5]	7.4 [6.0-7.7]	5.6 [5.3-5.8]
	HR [95% CI], p-value	**0.55** [0.34-0.88], 0.0105	..	**0.69** [0.58-0.83], <0.0001	..
DoR (months)	Median [95% CI]	11.2 [7.4-NE]	5.4 [2.0-6.8]	7.3 [5.8-7.6]	5.0 [3.8-5.6]
	HR [95% CI], p-value	**0.22** [0.08-0.62], 0.0035	..	**0.67** [0.48-0.93], n/a	..

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DoR duration of response. Gem/Nab gemcitabine/nab-paclitaxel standard of care. OS overall survival. PFS progression free survival. [1]Wainberg (2023) Lancet 402:1272. NALIRIFOX leucovorin+ 5-FU+liposomal irinotecan+oxaliplatin

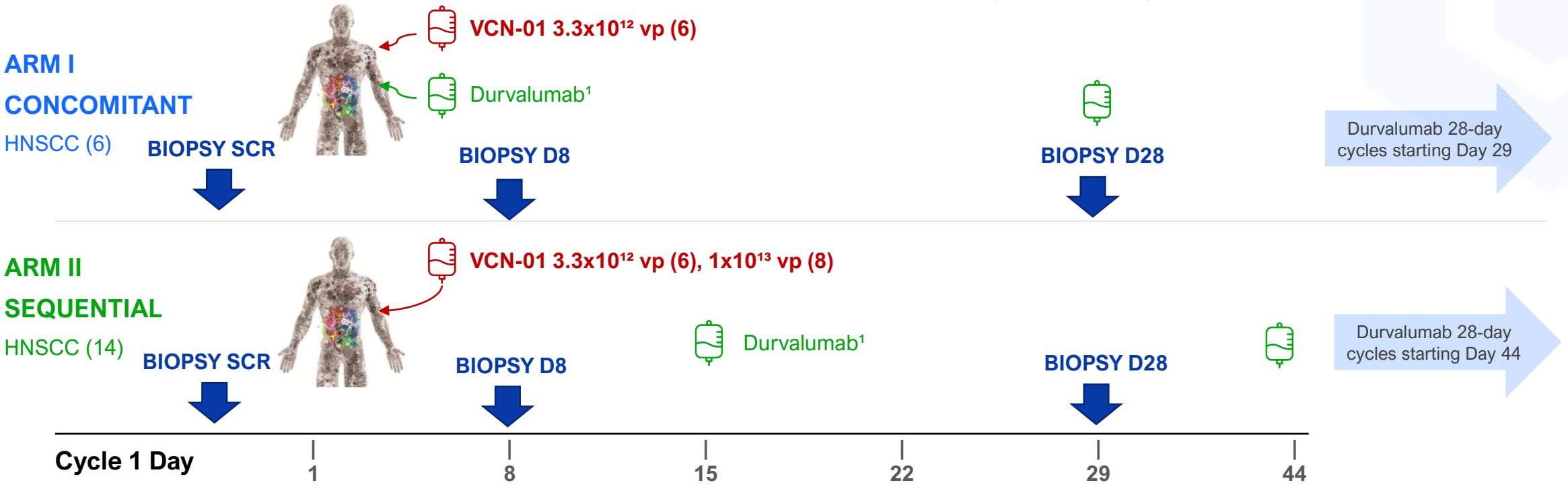
Theriva BIOLOGICS

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



Theriva BIOLOGICS

[1]Durvalumab 1500 mg (60 min infusion) administered at least 4 hours after VCN-01. HNSCC head and neck squamous cell carcinoma.
Jové M (2023) Ann Oncol 34:S589–S590.

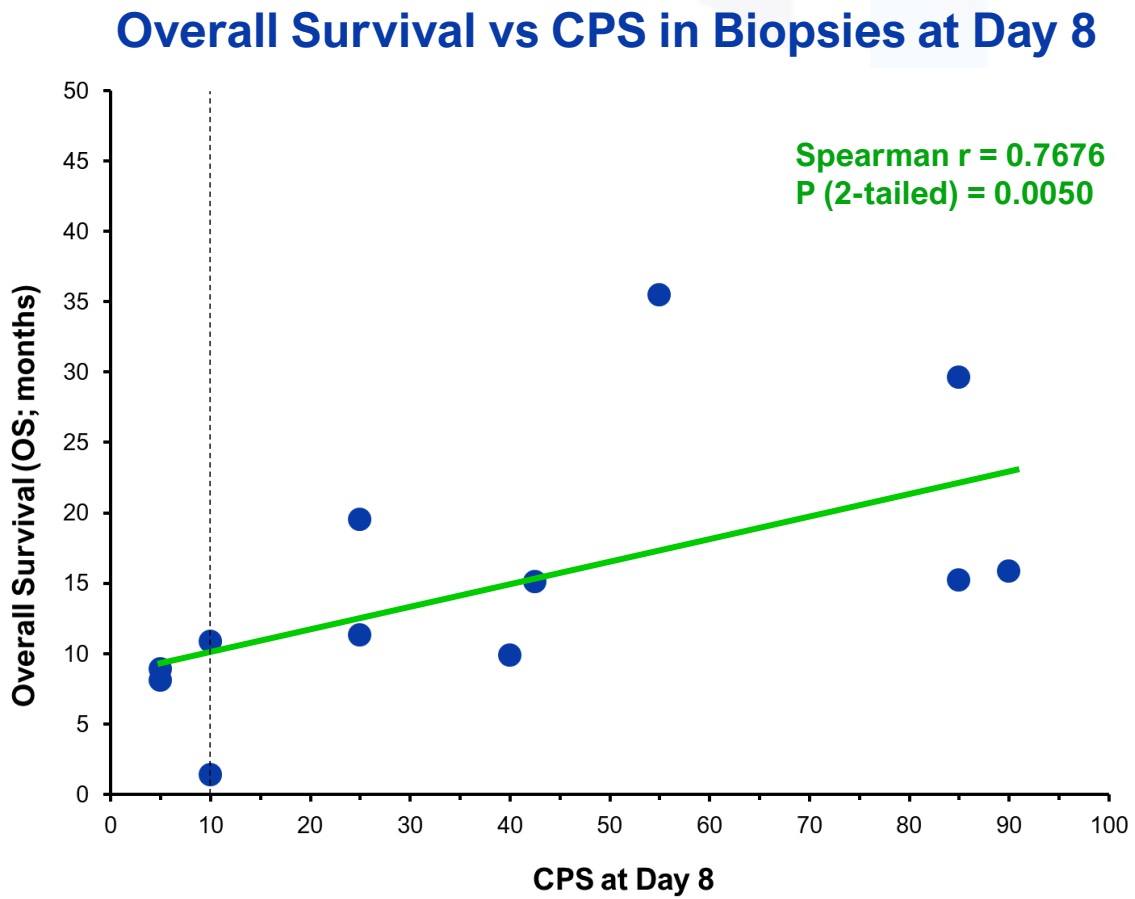
EXTENDED SURVIVAL with VCN-01+DURVALUMAB

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	
	$3.3x10^{12}$ vp	$1.0x10^{13}$ 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



Theriva BIOLOGICS

ESMO Congress 2023 Poster 937P: Survival Outcomes in Phase I Trial Combining VCN-01 and Durvalumab (MEDI4736) in Subjects with Recurrent/Metastatic Head and Neck Squamous Cell Carcinoma Refractory to Previous Immunotherapy Treatment. Jové M (2023) Ann Oncol 34:S589

VCN-01 MAY SENSITIZE PATIENTS TO SUBSEQUENT THERAPY

Patients responded to subsequent chemotherapy after progressing with VCN-01 + durvalumab

ARM	ICI Treatment Progression (Pre-trial)	Current Trial			1st Line after Current Trial	2nd Line after Current Trial
	Median OS post-1st ICI	ORR	Median PFS	Median OS	ORR	ORR
Concomitant Low (3.3E12vp)	21.6 (19.2-NE)	0/6	1.7 (1.6-NE)	10.4 (8.9-NE)	3/5	1/2
Sequential Low (3.3E12vp)	23.9 (16.6-NE)	1/6	3.7 (2.2-NE)	15.5 (15.1-NE)	3/6	1/6
Sequential High (1E13vp)	21.8 (12.9-NE)	0/6	2.1 (1.4-NE)	17.3 (11.3-NE)	2*/5	1/4

*Complete Responses

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AE PROFILE FOR THE COMBINATION OF VCN-01 AND DURVALUMAB

Most common AEs related to IV VCN-01 [NCT03799744]

Adverse Reactions	Arm I - Concomitant (Dose 3,3E12 , n=6)[2]		Arm II - Sequential (Dose 3,3E12 , n=6)[3]		Arm II - Sequential (Dose 1E13 , n=8)[3]	
CTCAE Grade	Grade 1-2	Grade ≥3	Grade 1-2	Grade ≥3	Grade 1-2	Grade ≥3
Pyrexia	2 (33,0%)	-	5 (62,5%)	-	3 (50%)	-
Influenza like illness	3 (50,0%)	-	3 (37,5%)	2(25%)	2 (33,3%)	-
Asthenia/Fatigue	2 (33.0%)	-	2 (25%)	1 (12,5%)	4 (66,6%)	-
AST increased	4 (66,7%)	1 (16,6%)	2 (25%)	-	-	2 (33,3%)
ALT increased	3 (50,0%)	1 (16,6%)	1 (12,5%)	-	-	2 (33,3%)
Decreased Apetite	1 (16,6%)	-	3(37,5%)	-	2 (33,3%)	-
Lymphocyte count decreased	1 (16,6%)	-	-	3 (37,5%)	-	-
Myalgia	-	-	3(37,5%)	-	1 (16,6%)	-
Hypotension	-	-	2 (25%)	-	1 (16,6%)	-
Chills	1 (16,6%)	-	1(12,5%)	-	1 (16,6%)	-
Vomiting	1 (16,6%)	-	1(12,5%)	-	1 (16,6%)	-
Anemia	2 (33,0%)	-	1(12,5%)	-	1 (16,6%)	-
Nausea	-	-	1(12,5%)	-	1 (16,6%)	-
Headache	-	-	1(12,5%)	-	1 (16,6%)	-
Erythema	1 (16,6%)	-	1(12,5%)	-	-	-
Guillain-Barre Syndrome	-	1 (16,6%)	-	1 (12,5%)	-	-
Hepatic enzymes increased	-	-	-	1 (12,5%)	-	-
GGT Increased	-	-	-	-	-	1 (12,5%)

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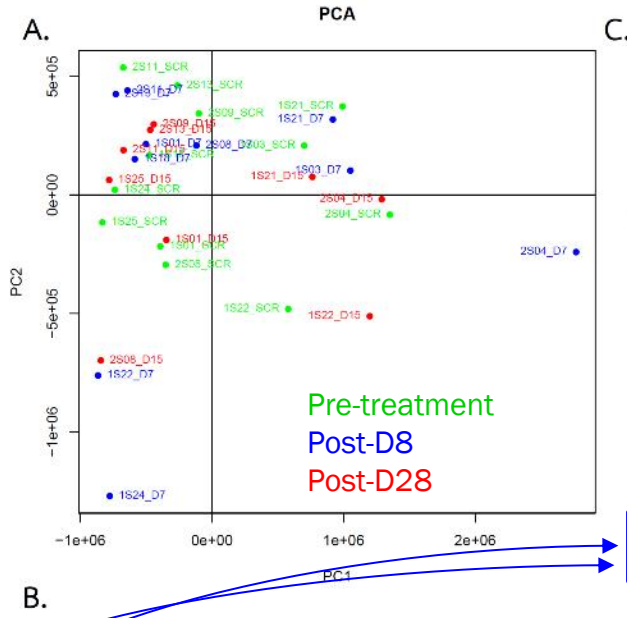
VCN-01 INDUCES TRANSCRIPTOMIC CHANGES in TUMOR MICROENVIRONMENT

RNAseq Analysis in Clinical Samples from HNSCC Patients [NCT03799744]

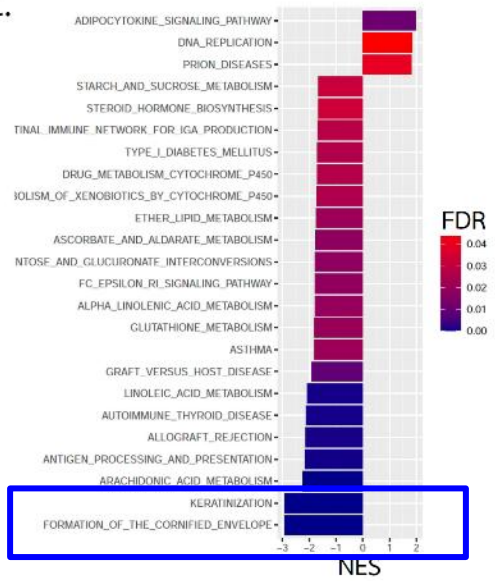
Principal Component Analysis[1]

including all the Pre- and Post-treatment samples

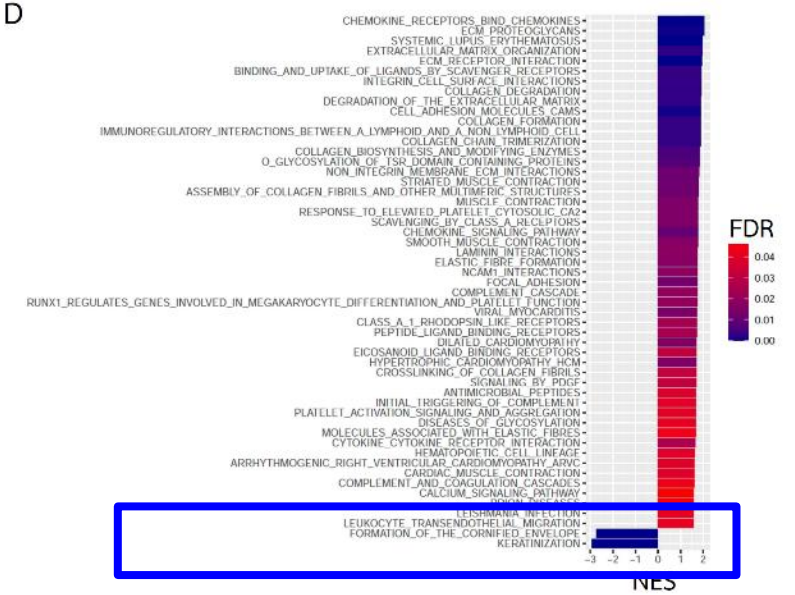


Most significant Reactome and KEGG pathways in GSEA (Gene Set Enrichment Analysis) [1]

analysis D8 vs Pre-treat.



analysis D28 vs Pre-treat.



B.

Gene	Gene product	log2FoldChange	padj	
CIDEC	Cell Death Inducing DFFA Like Effector C	5.524	0.047	Up D7
TAGLN3	Transgelin 3	1.615	0.037	
GPR3	G Protein-Coupled Receptor 3	1.157	0.039	
ABP1	Auxin-binding protein 1	-1.636	0.013	Down D7
CD207	CD207 Molecule	-1.960	0.044	
MEGF10	Multiple EGF Like Domains 10	-2.008	0.043	
OSTalpha	Organic solute transporter alpha	-2.179	0.039	
CD1E	CD1E Molecule	-2.316	0.010	
ATP10B	ATPase Phospholipid Transporting 10B	-2.556	0.044	
FCER1A	Fc Epsilon Receptor Ia	-2.687	0.006	
LOC285629	.....	-2.818	0.001	
LCE1B	Late Cornified Envelope 1B	-7.921	0.006	

Sustained differential gene expression profiles associated with downregulation of matrix-related pathways

Jové M et al. (2022) Poster 1231P: European Society for Molecular Oncology conference ESMO2022, 12 September 2022

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

Theriva BIOLOGICS

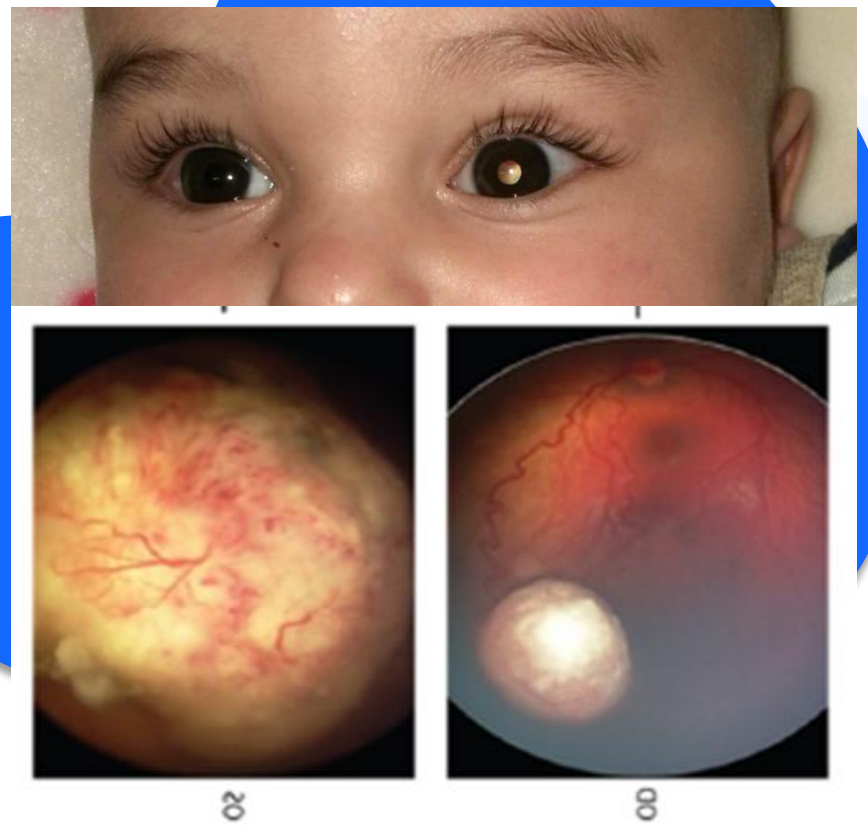
ESMO Congress 2022 Poster 1231P: Phase I Study to Evaluate the Safety, Tolerability, and Efficacy of VCN-01 in Combination With Durvalumab (MEDI4736) in Subjects With Recurrent/ Metastatic Squamous Cell Carcinoma of the Head and Neck (R/M HNSCC). Jove M (2022) Ann Oncol 33:S1112.
IDO Indoleamine-2,3-dioxygenase.

Theriva BIOLOGICS

VCN-01 IN RETINOBLASTOMA

RETINOBLASTOMA, A RARE PEDIATRIC MALIGNANCY

- Retinoblastoma (Rb) is an orphan indication that accounts for ~2-3% of all childhood cancers[1]
- 200-300 cases each year in the USA, EU[2-4]
- 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



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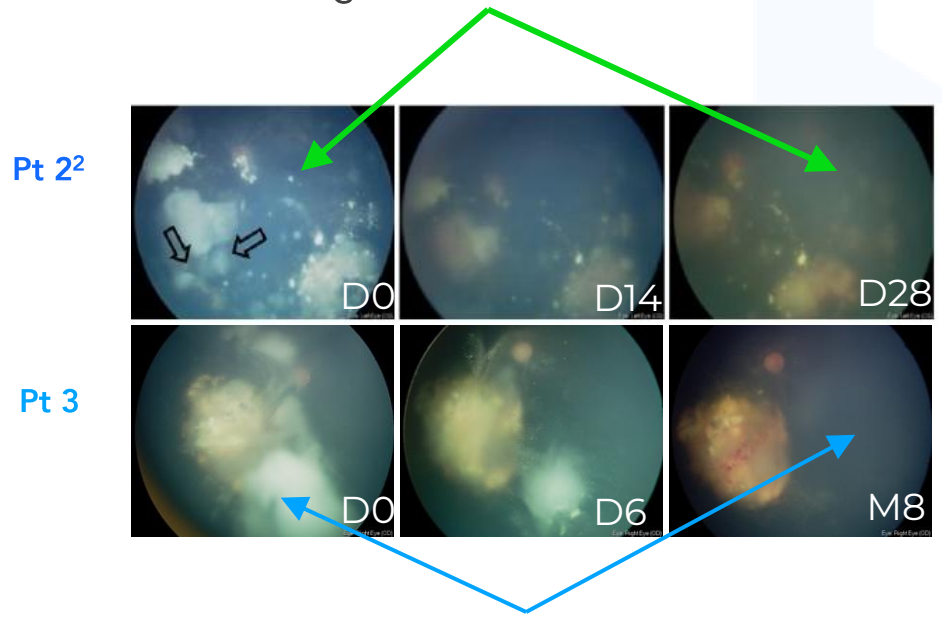
[1]https://www.cancer.org/cancer/retinoblastoma/about/key-statistics.html. [2]Stacey (2021) Ophthalmology 128:1369. [3]One Retinoblastoma World Map https://map.1rbw.org/. [4]For additional details and references see Appendix. IMAGE: Courtesy of Hospital Sant Joan de Déu, Barcelona

VCN-01 IN RETINOBLASTOMA

- Single center, open-label, dose escalation study of intravitreal (IVit) VCN-01[1-3]
  - 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 $2.0x10^9$ vp per eye (n=1) or $2.0x10^{10}$ 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[2]



Complete tumor regression[3]

[1]NCT03284268. [2]Pascual Pasto (2019) Sci Transl Med 11:eaat9321. [3]Data presented at International Oncolytic Virus Conference IOVC2021, 07 November 2021, Sedona, AZ. Link to IOVC2021 slide deck provided in Appendix. RP2D recommended phase 2 dose. vp virus particles.

ADVERSE EVENT DATA FOR INTRAVITREAL VCN-01

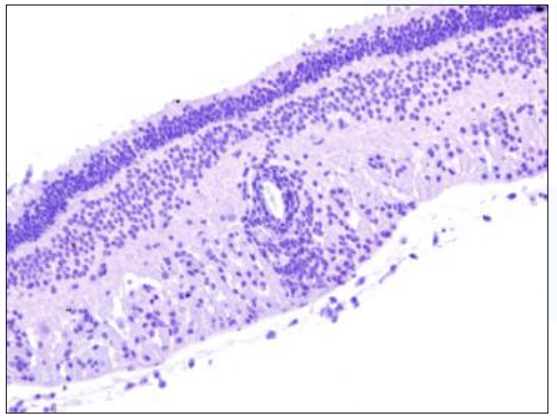
Two Intravitreal VCN-01 Doses of $2.0x10^9$ or $2.0x10^{10}$ vp per eye[1]

Adverse Reaction	Pts	All Grades		Grade ≥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%

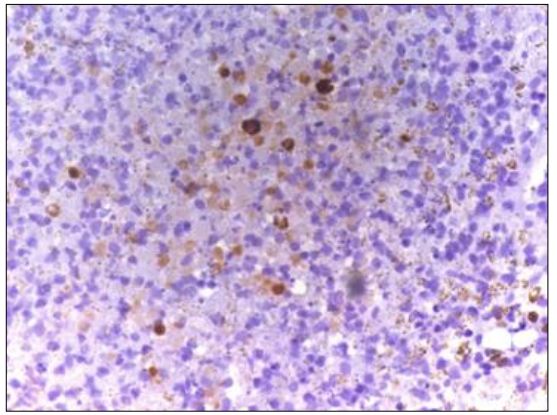
- VCN-01 was reasonably well tolerated after intravitreal administration[2], although some turbidity and uveitis associated with intravitreal inflammation was observed
- Intravitreal inflammation was managed with local and systemic administration of anti-inflammatory drugs
- VCN-01 induced reversible 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[3]

Selective expression of viral proteins

Conserved retina



Necrotic tumor



Theriva BIOLOGICS

[1]NCT03284268. [2]Intravitreal VCN-01 doses of $2.0x10^9$ virus particles (vp) per eye (Patient 1) or $2.0x10^{10}$ vp per eye (Patients 2-4) administered on days 1 and 15. [3]Pascual Pasto (2019) Sci Transl Med 11:eaat9321. Data presented at International Oncolytic Virus Conference IOVC2021, 07 November 2021, Sedona, AZ.

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
  - Refractory retinoblastoma patients with vitreous seeds
  - IVit VCN-01 in combination with topotecan
  - PI Dr. Guillermo Chantada, MD PhD[1]
- 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)

Theriva BIOLOGICS

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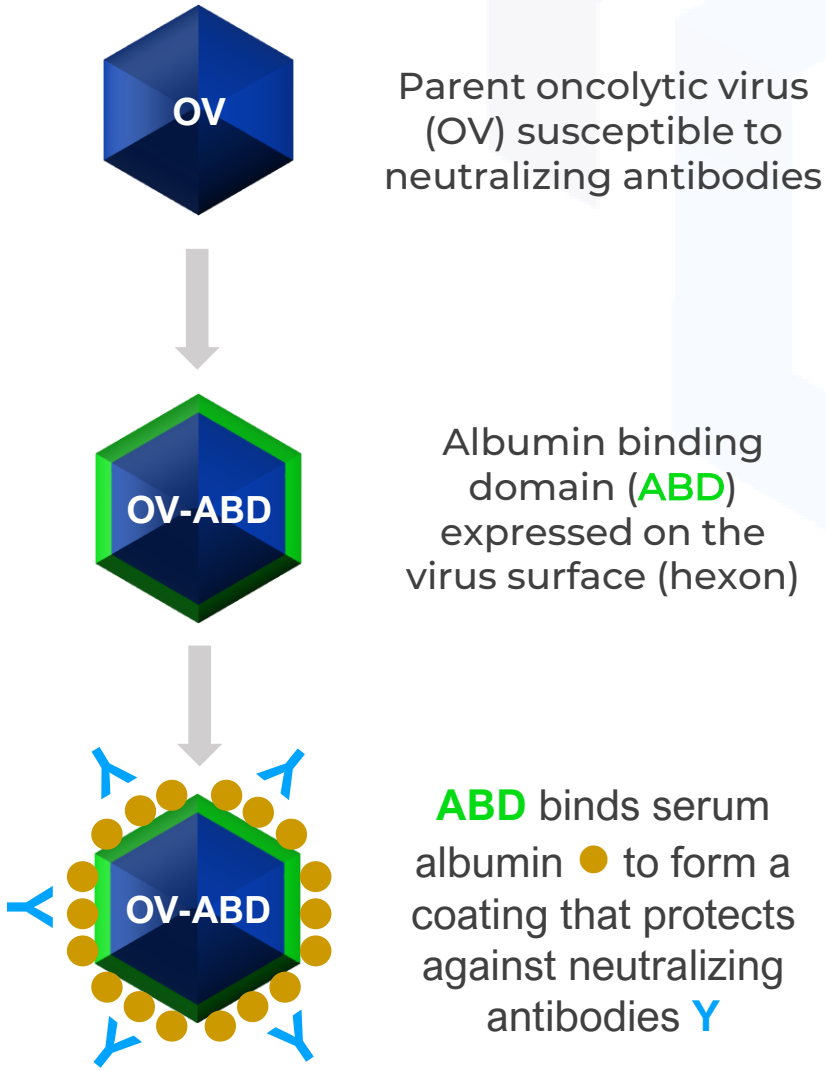
Theriva BIOLOGICS

VCN-X NEXT GENERATION OV DISCOVERY PLATFORM

ALBUMIN SHIELD™ to ENHANCE OV SYSTEMIC DELIVERY

- Albumin Shield technology protects OVs as they travel to tumors after systemic administration[1,2]
- 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



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