

Unique Oncolytic Virus Therapies for Multiple Solid Tumors

May 2026



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, 2025 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.






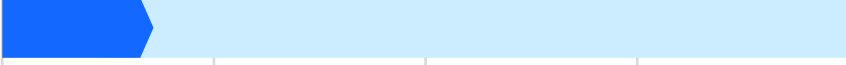




OVERVIEW

- **VCN-01** lead candidate undergoing **Phase 3** clinical trial preparation¹
 - First-line metastatic pancreatic cancer
 - Retinoblastoma (rare pediatric disease)
- **VCN-01** Phase 1 clinical data support potential in additional indications²
- **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 (31Mar2026)	\$14.4M
Projected cash runway	Q1 2027
Average Daily Volume (3M)	27.1M ³
Locations	Rockville, MD Barcelona, Spain

THERIVA CURRENT 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)					 HOSPITAL MATERNOINFANTIL UNIVERSITAT DE BARCELONA	Planning Phase 2/3 Orphan Drug Designation US, EU Rare Pediatric Disease Designation US
	Brain tumors (IV)					 LEEDS	Phase 1 On-going
VCN-X and Albumin Shield OVs	Solid tumors (IV)					 	Preclinical Studies On-going
SYN-004 ^[1] Oral β -lactamase	Prevention of aGVHD in allo-HCT						Phase 1b/2a On-going

VCN-01 IS A UNIQUELY ENGINEERED HUMAN ADENOVIRUS 5

Designed to have multiple anti-tumor actions

Systemic

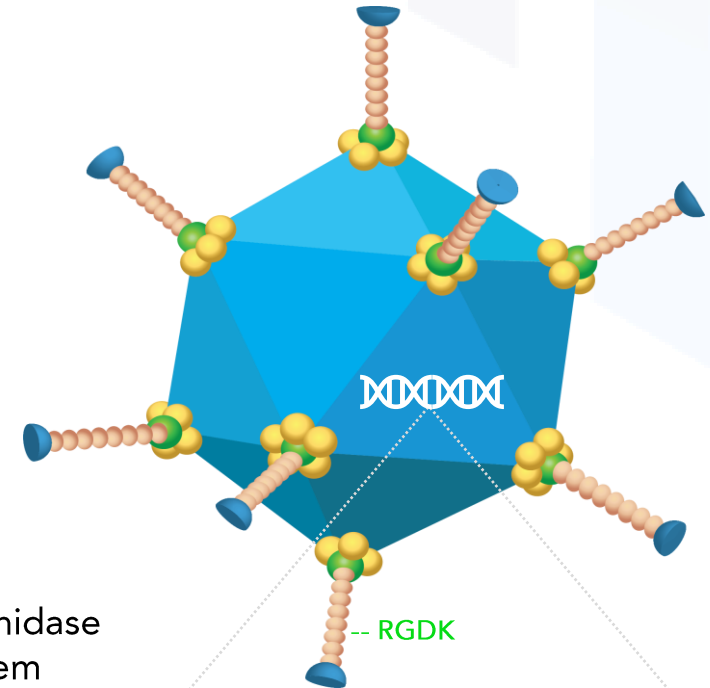
VCN-01 targets both **primary** and **metastatic** lesions

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

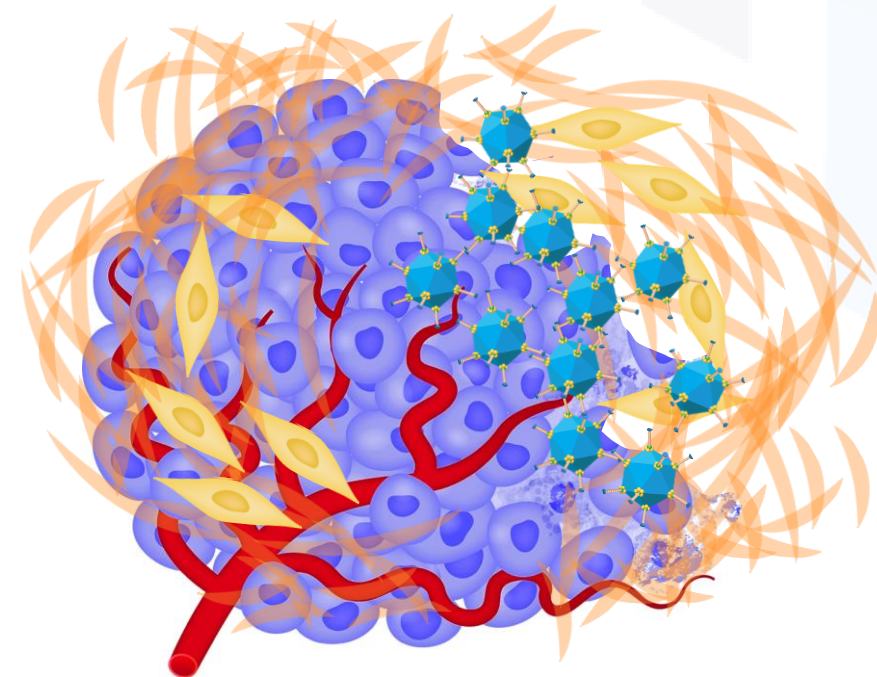
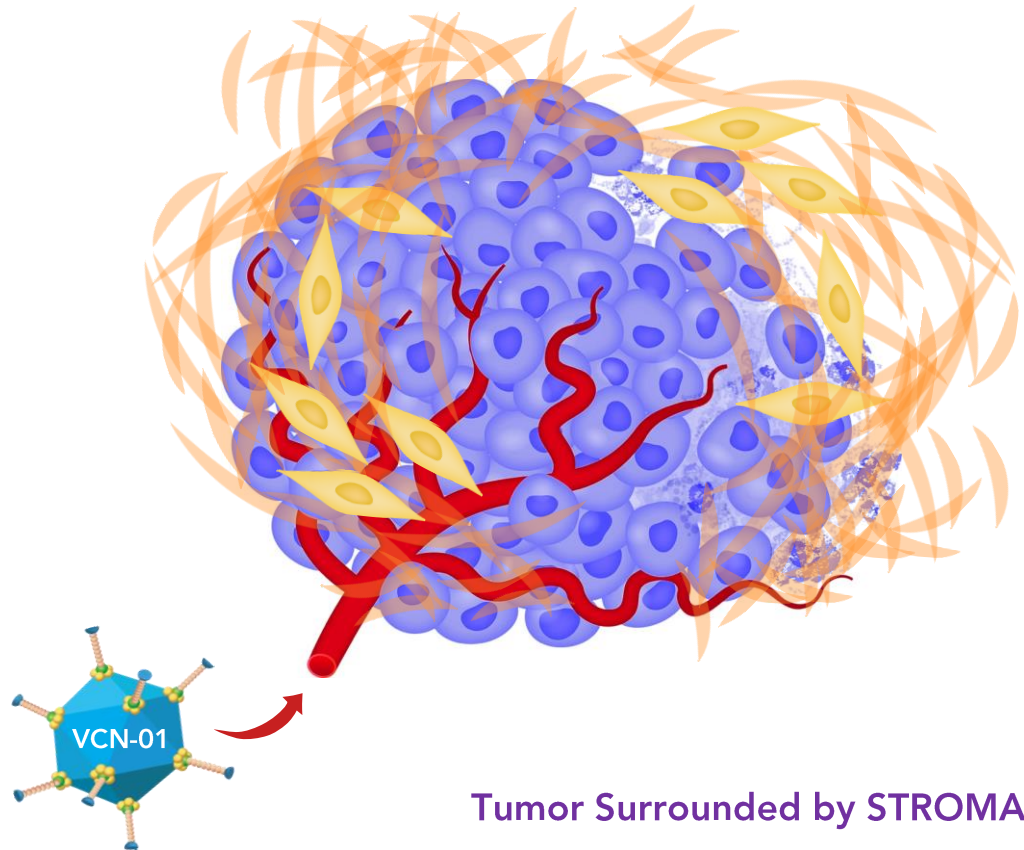


E2F binding +++ → E1a-Δ24 → MLP → PH20

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



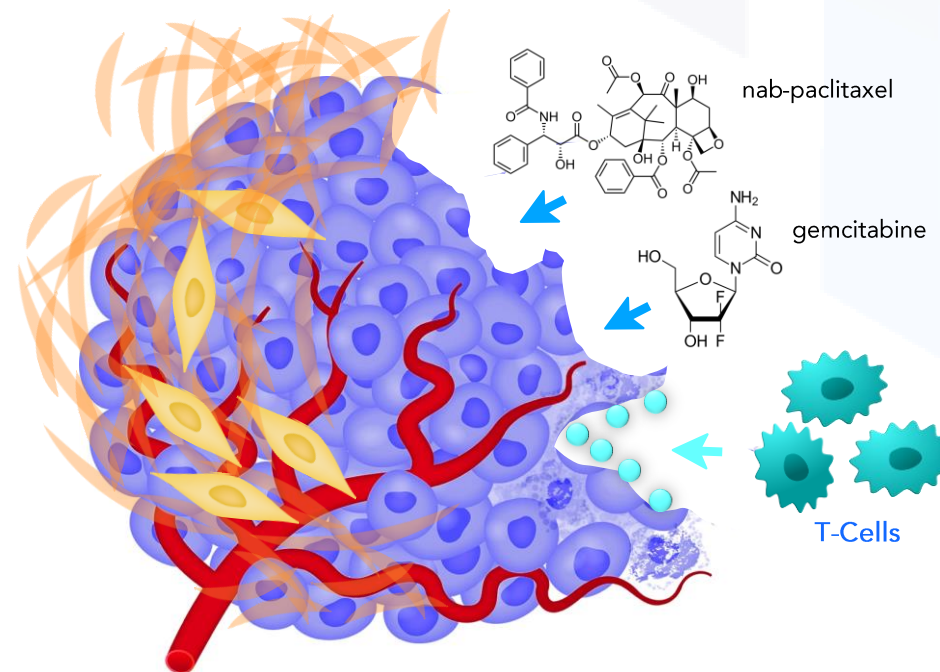
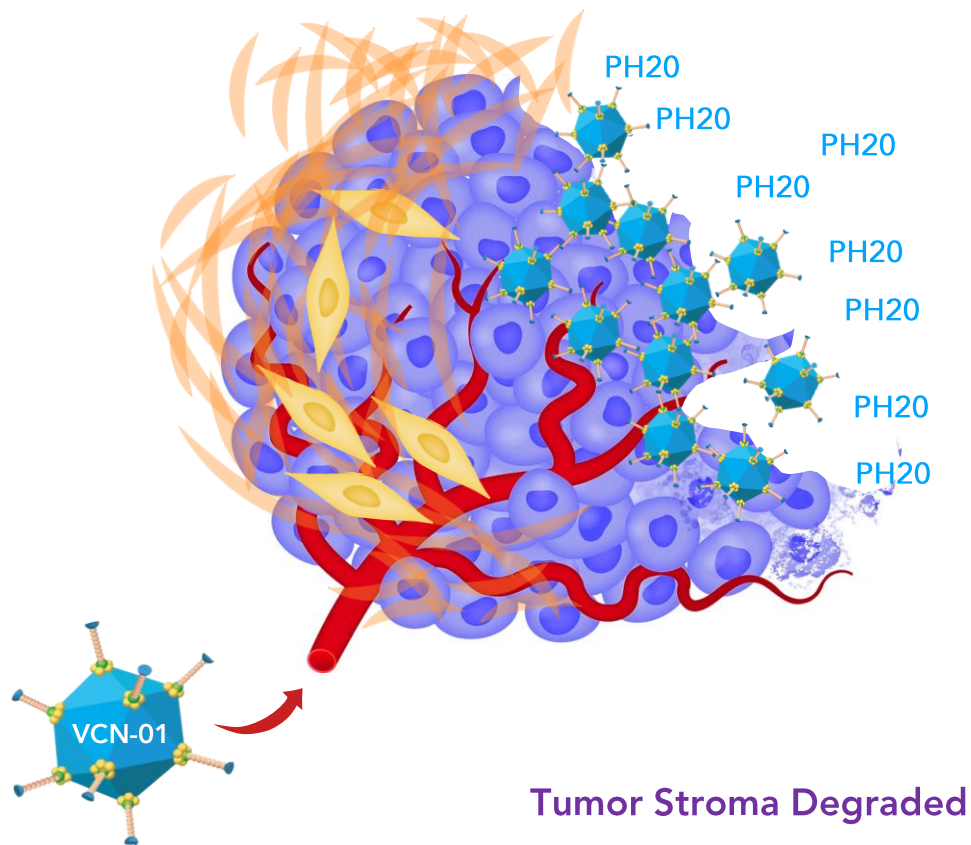
Tumor Surrounded by STROMA



VCN-01 DESIGNED TO HAVE MULTIPLE ANTI-TUMOR ACTIONS

3 **STROMA** degradation by PH20 facilitates solid tumor access and destruction by coadministered cancer therapies

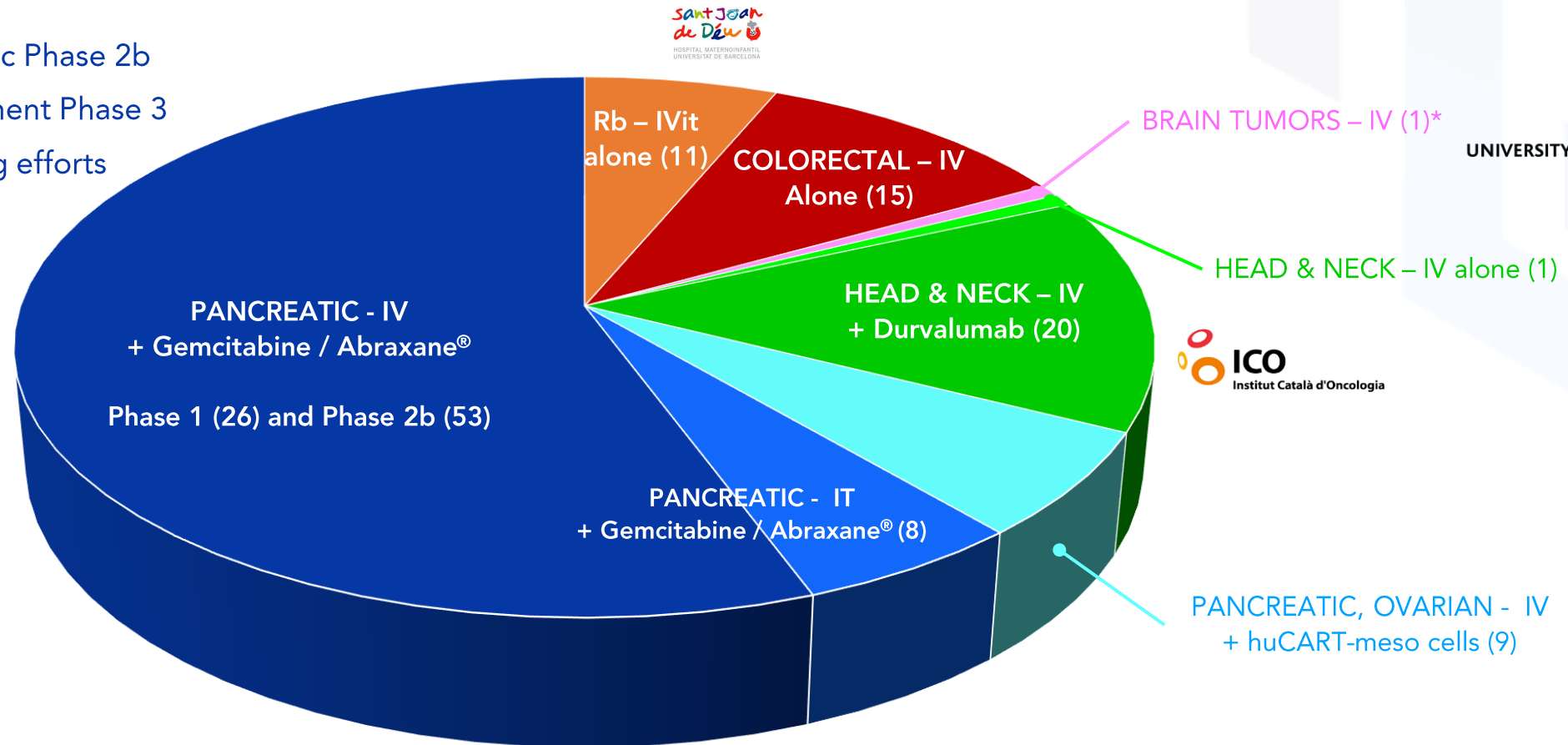
4 **IMMUNOGENIC** actions of VCN-01 turn "cold" tumors "hot" and elicit an anti-tumor immune response



VCN-01 EXTENSIVE CLINICAL EXPERIENCE

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

- Successful pancreatic Phase 2b
- EMA & FDA agreement Phase 3
- On-going partnering efforts



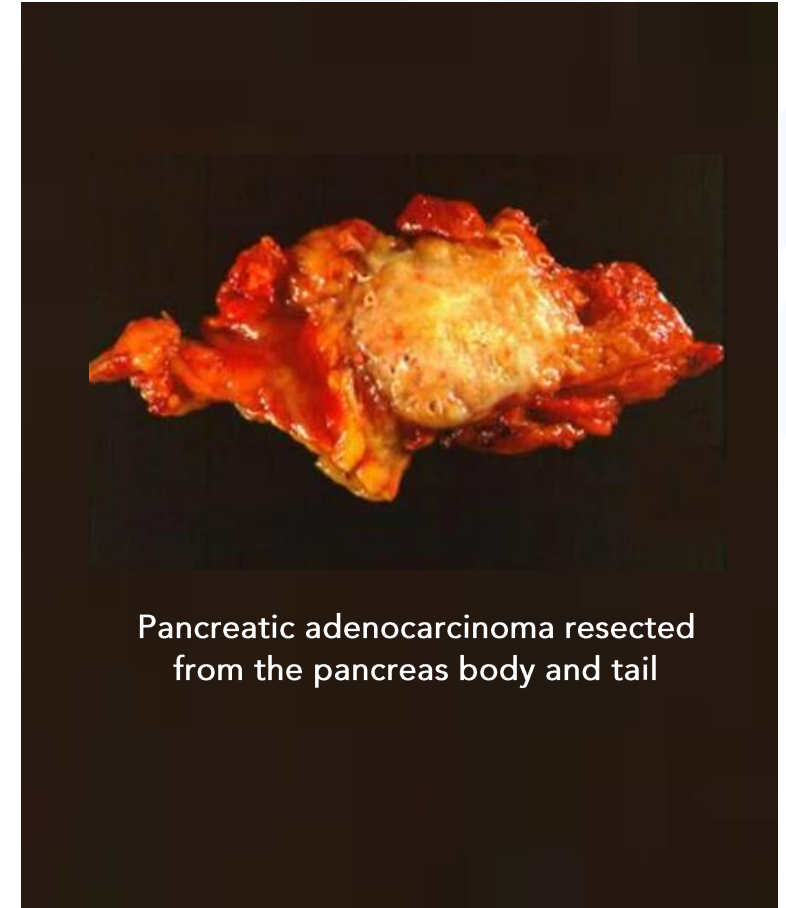
(Number of VCN-01 Patients Treated in Parentheses)



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 2025³
- **Hyaluronic acid** in stroma is associated with reduced treatment efficacy and poor prognosis⁴
 - VCN-01 designed to degrade hyaluronic acid
- Incidence is growing worldwide
 - Est. treatment market ~\$2.9B (2024) ~\$6.0B (2030)⁵

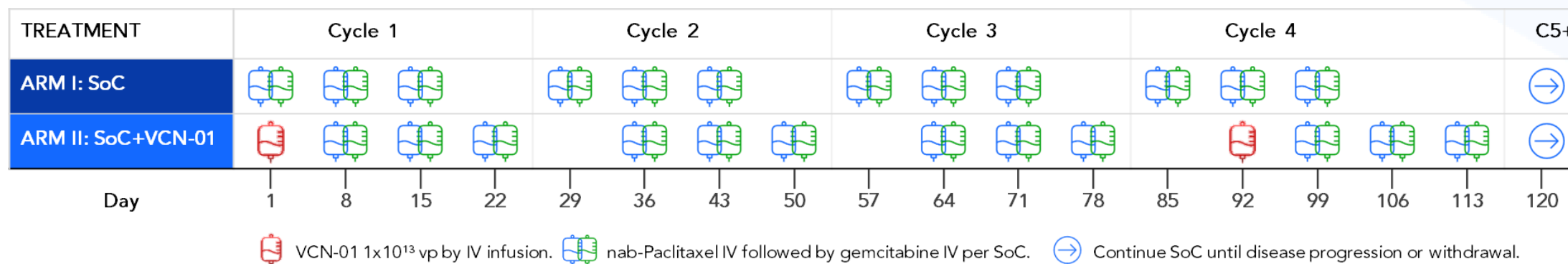


Pancreatic adenocarcinoma resected from the pancreas body and tail

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



Main Analysis



Subgroup Analysis (Started Cycle 4; 2 doses of VCN-01)



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)
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)

¹Full Analysis Set (FAS) patients received at least 1 dose of gemcitabine/nab-paclitaxel (SoC) in each arm.

²Compares 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.

VIRAGE TREATMENT EMERGENT ADVERSE EVENTS

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

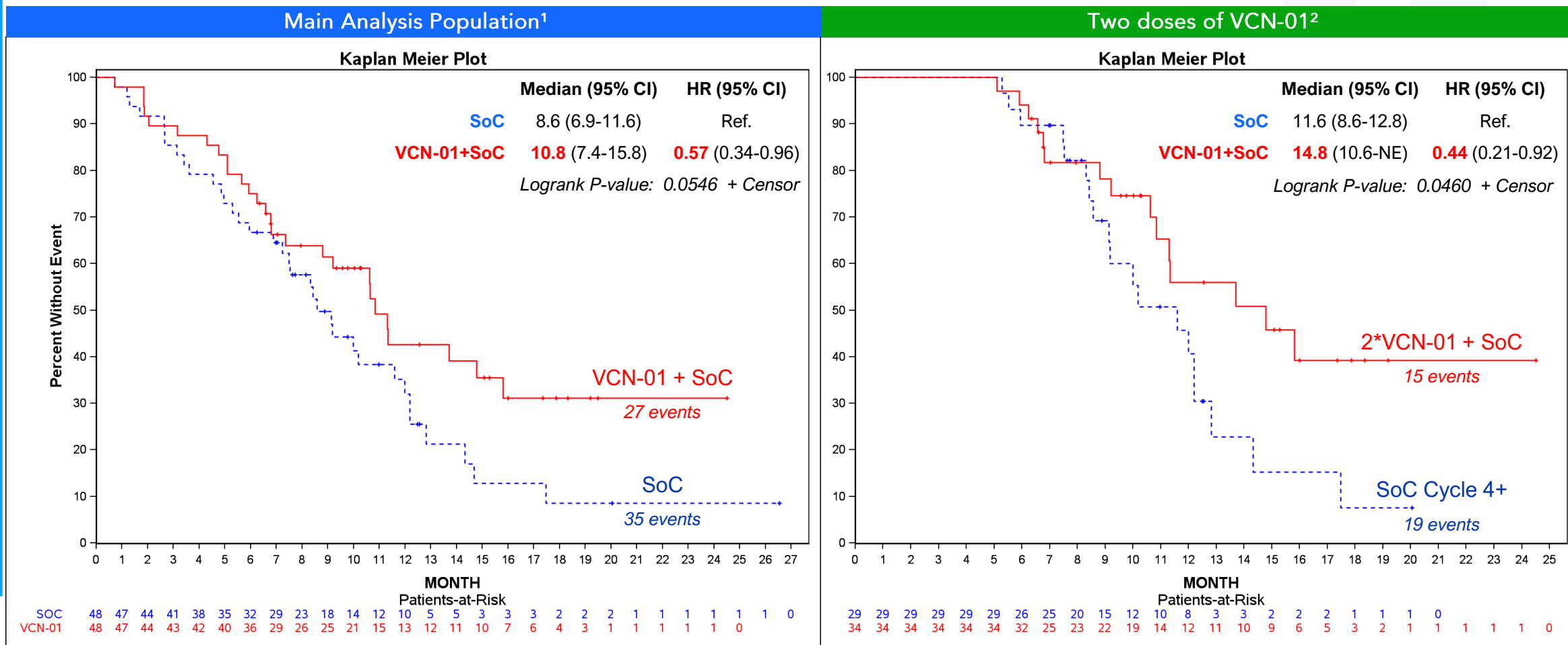
Preferred Term – No. Patients (%) ^{a,b}	All Grades		Grade 3-4	
	First Dose (n=53)	Second Dose (n=36)	First Dose (n=53)	Second Dose (n=36)
Pyrexia	31 (58.5%)	19 (52.7%)	1 (1.9%)	-
Nausea	16 (30.2%)	6 (16.6%)	-	-
Asthenia	15 (28.3%)	4 (11.1%)	1 (1.9%)	1 (2.8%)
Vomiting	14 (26.4%)	9 (25.0%)	-	-
Aspartate 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%)

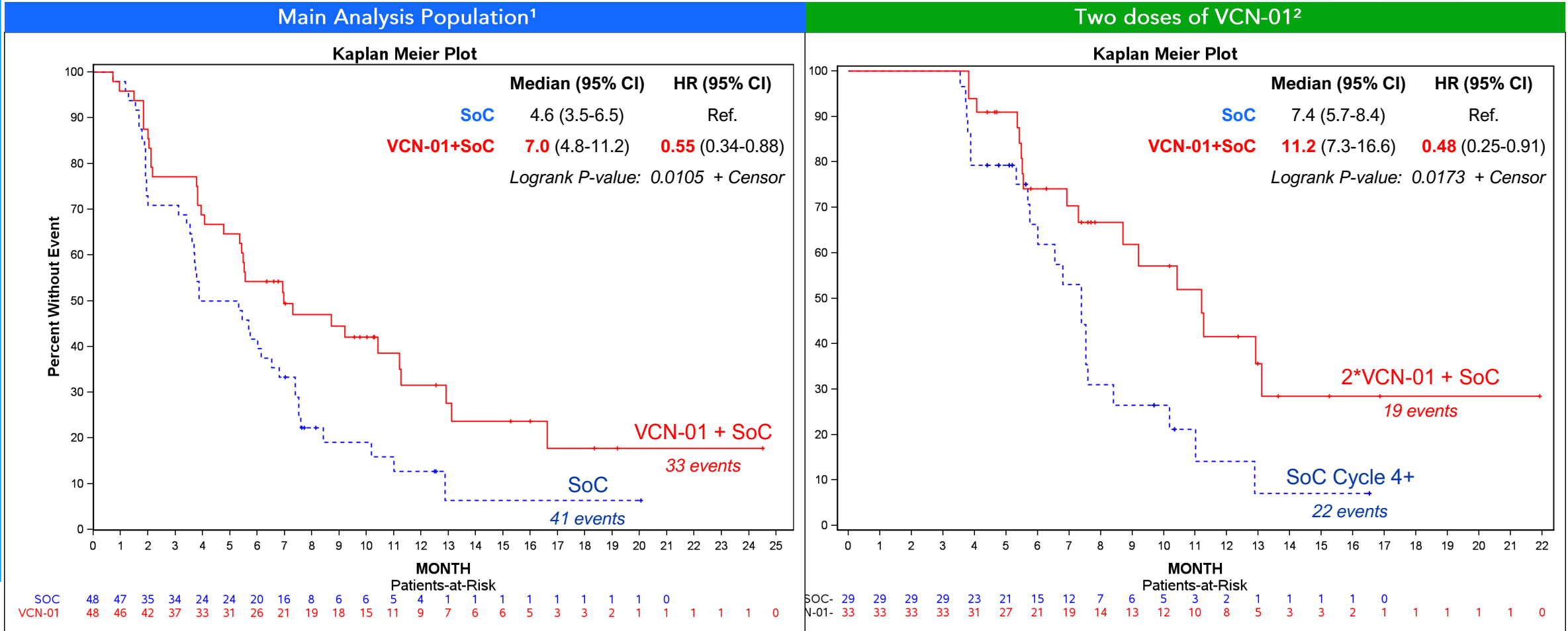
INCREASED OVERALL SURVIVAL IN VCN-01+SOC ARM

Greater OS improvement with two VCN-01 doses



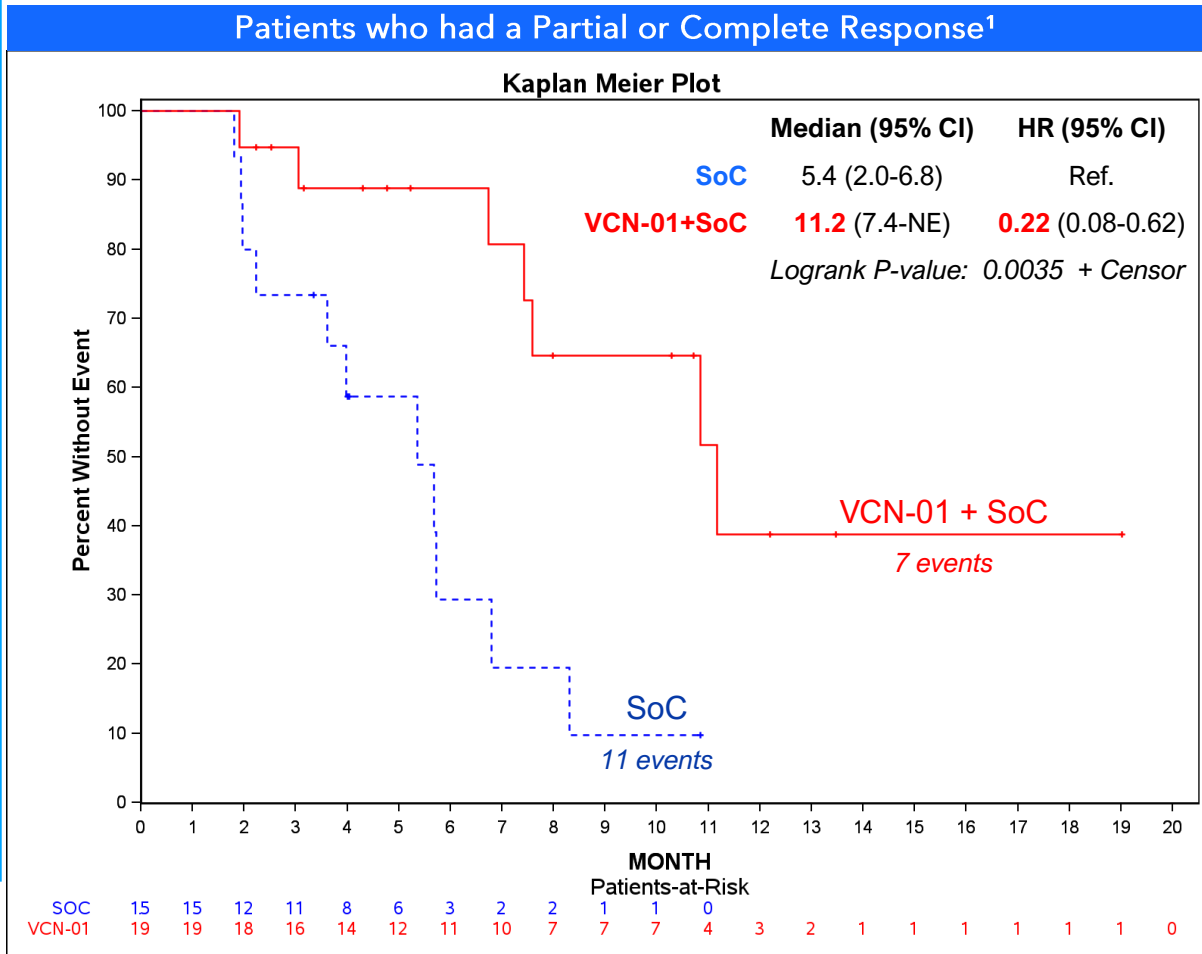
INCREASED PROGRESSION-FREE SURVIVAL IN VCN-01+SOC ARM

Greater PFS improvement with two VCN-01 doses



DURATION OF RESPONSE DOUBLED IN VCN-01+SOC ARM

Increased response rate with two VCN-01 doses

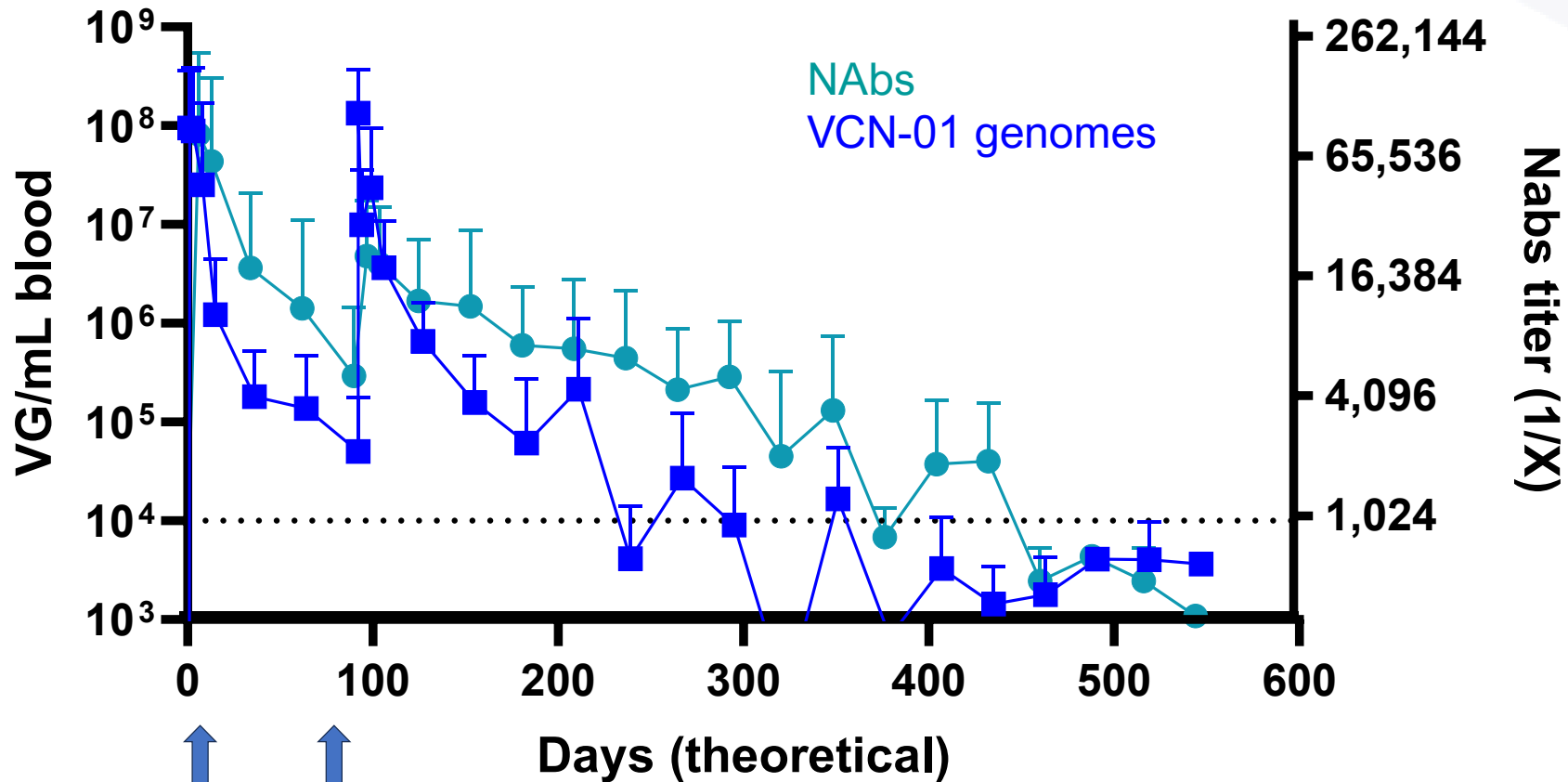


Objective Response Rates (ORR)¹

	Main Analysis (FAS) ¹		Subgroup (2 Doses VCN-01) ²	
	SoC	VCN-01 + SoC	SoC C4+	2*VCN-01 + SoC
N (%)				
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%)
		<i>p=0.314</i>		<i>p=0.533</i>

VIRAGE BIOLOGICAL DATA SUPPORT REPEAT DOSING

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



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 trial¹

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 “macrocycles” comprising 1 IV dose of VCN-01 (1×10^{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

	Macrocycle 1 (MC1)												Repeat Macrocycles to Progression						
TREATMENT	IMP	Gem-Nab SoC			Gem-Nab SoC			Gem-Nab SoC			MC2	MC3	MC4+						
ARM I: SoC+Placebo												 	 	 					
ARM II: SoC+VCN-01												 	 	 					
Day	1	8	15	22	29	36	43	50	57	64	71	78	85	92	99	183	190	274	281

 Placebo (saline) IV infusion
  VCN-01 1×10^{13} vp by IV infusion.
  nab-Paclitaxel IV followed by gemcitabine IV per SoC.
  Gem-Nab SoC 3 x 28-day cycles

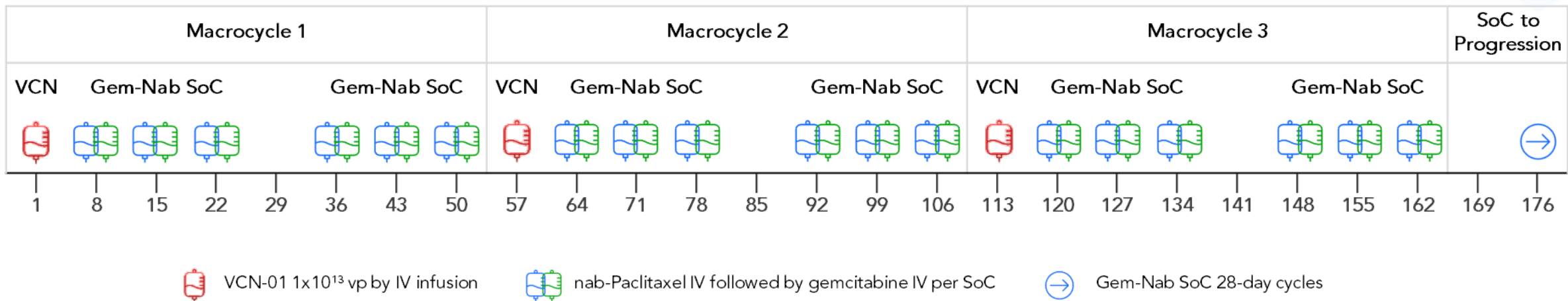
REGULATORY ALIGNMENT ON PHASE 3 TRIAL DESIGN

FDA and EMA agreement on critical protocol elements

- **Agreed** on proposed inclusion/exclusion criteria, study arms, primary endpoint (OS) and secondary endpoints (including PFS, ORR)
- **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/BLA
- **Recognized** the survival benefit of the second VCN-01 dose in the VIRAGE trial
- **Recommended** removing the week off between macrocycles and considering more frequent dosing¹

VCN-01 ADDITIONAL PDAC CLINICAL ACTIVITIES

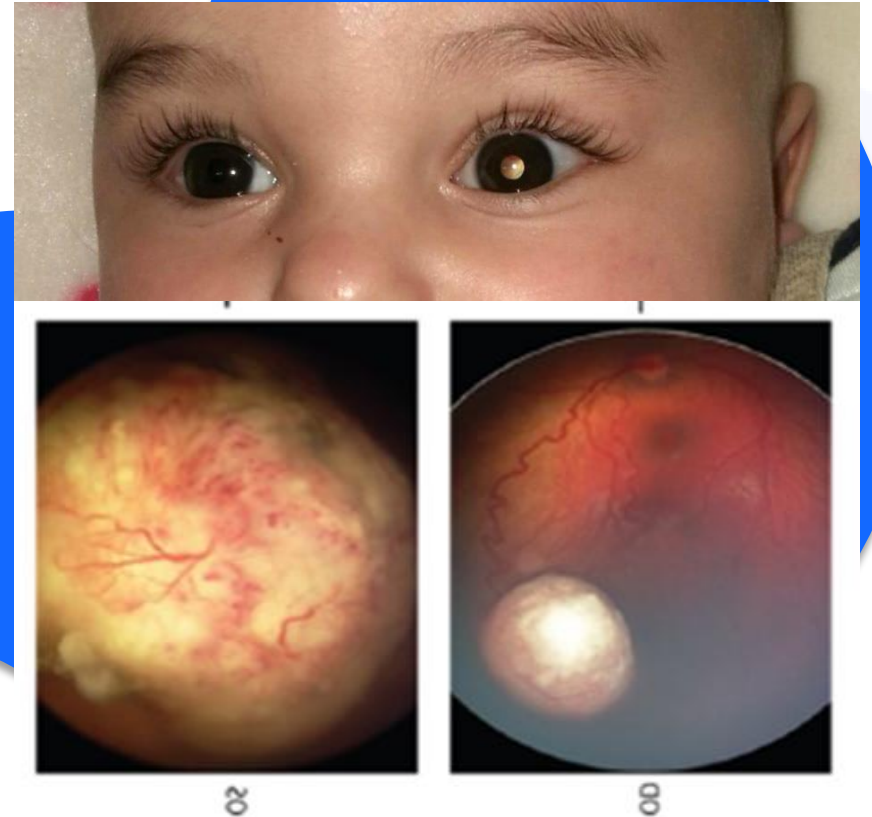
- Phase 2a study to explore feasibility of more frequent VCN-01 dosing to potentially improve outcomes in a Phase 3 trial
 - Small (n=6 evaluable), single-arm, open-label study at a single center in Spain
 - VCN-01 administered every 2 months (up to 3 doses) in combination with SoC chemotherapy¹
 - Primary endpoints safety/tolerability, VCN-01 pharmacokinetics
 - Secondary endpoints survival (OS, PFS), response (ORR, DoR), circulating anti-VCN-01 NAb



RETINOBLASTOMA, A RARE PEDIATRIC MALIGNANCY

Potentially lower-cost pathway to market

- Retinoblastoma (Rb) is an ultrarare orphan indication that accounts for 2-3% of all childhood cancers¹
 - 200-300 cases each year in the USA, EU
 - >1,000 cases each year in India, China²⁻⁴
- VCN-01 designed for **intravitreal** administration with chemotherapy
- VCN-01 positioned as 3rd line for patients who fail standard therapy
 - Prevent eye enucleation; ideally preserve vision
 - No approved standard-of-care



VCN-01 DEVELOPMENT IN RETINOBLASTOMA

Leverage Rare Pediatric Disease Designation

- Phase 1 Investigator Sponsored Study Completed H1 2024
 - Data in last line/rescue patients demonstrated acceptable AE profile and 3 complete responses
- Finalizing a Phase 2-3 Protocol for Discussion with the FDA
 - Intravitreal VCN-01 plus intravitreal topotecan to treat refractory Rb patients with vitreous seeds
 - Expect a relatively small number of patients for potential pivotal trial
 - Data from VCN-01 compassionate use supports feasibility of proposed dosing regimen
- Key Value Proposition Lies in Potential Priority Review Voucher (PRV)
 - VCN-01 has US and EU Orphan Drug Designation and Rare Pediatric Disease Designation (RPDD)
 - PRV available to drugs with RPDD that are approved by 30 Sep 2029
 - PRV can be monetized (PRV sold for \$200M in January 2026)¹

VCN-01 PHASE 1 ISS Last-Line/Rescue Therapy

Promising antitumor activity

- Nine children ages 2-7 with refractory RB facing imminent enucleation
 - Anticipated eye survival 37-43 days
- VCN-01 **intravitreal** administration on Days 1 and 15
 - Additional eye conservative therapy administered if evidence of potential benefit
- Safety Visit at Day 42
 - Potential response evaluated by RB-RECIST
- Eye survival follow-up to Day 180+

ID	Dose (vp/eye) x Day	Response Day 42	Follow-Up
1	2E09 x D1, 15	SD	Enucleation (D44)
2	2E10 x D1, 15	PR	Enucleation (D62)
4	2E10 x D1, 15, 64	PR ¹	CR (>5 years)
5	2E10 x D1, 15	SD	Enucleation (D56)
8	2E10 x D1, 15	PR ¹	Enucleation (D170)
9	2E10 x D1, 15	PD	Enucleation (D37)
11	2E10 x D1, 15	PR ¹	CR (>1 year)
12	2E10 x D1	PR ¹	CR (>1 year)
13	2E10 x D1, 15	SD ¹	Enucleation (D93)

¹Administered additional eye conservative therapy. CR complete response. D day. PD progressive disease. PR partial response. SD stable disease. Primary VCN-01 related AE uveitis managed with immunosuppressants.

SAFETY DATA PHASE1 TRIAL OF VCN-01 in RB

Adverse reactions (events associated with VCN-01, monotherapy)

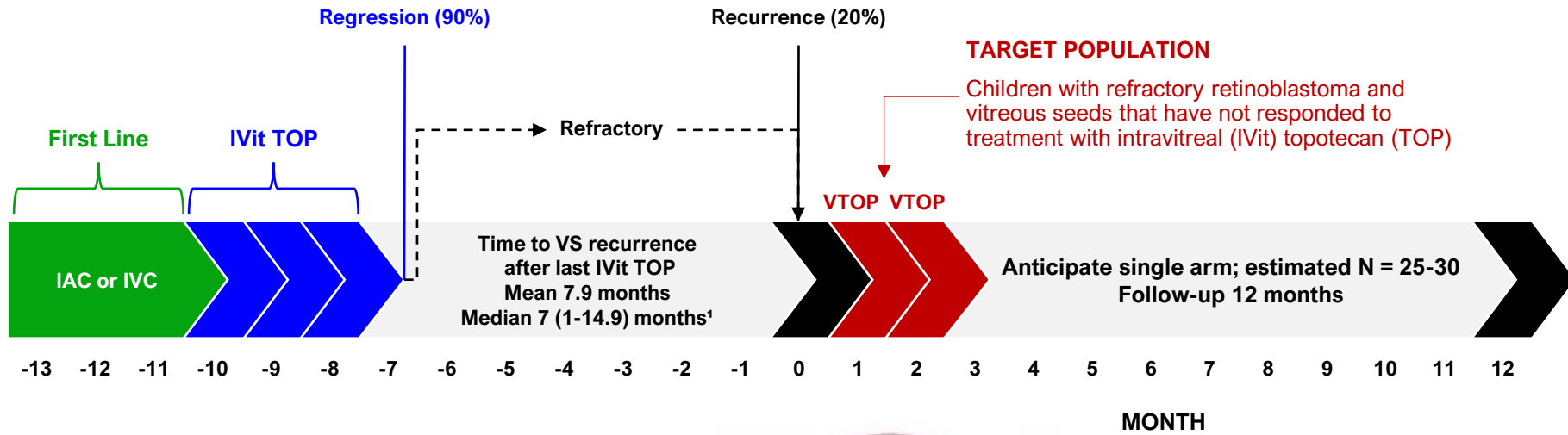
MedDRA System Organ Class (SOC)	Description/Nature of the event (MedDRA PT)	All Grades		Grade 3	
		n	%	n	%
Eye disorders	Uveitis	7	78%	4	44%
Eye disorders	Palpebral edema	1	11%	0	0%
Eye disorders	Conjunctival hyperemia	1	11%	0	0%
Eye disorders	Iridocyclitis (eye inflammation)	1	11%	0	0%

Serious Adverse Events

MedDRA System Organ Class (SOC)	Description/Nature of the event (MedDRA PT)	VCN-01 Relatedness	Number events
Eye disorders	Uveitis*	Related	3
Eye disorders	Retinal detachment	Non-related	1
Eye disorders	Hyphema	Non-related	1
Eye disorders	Eye excision (enucleation)	Non-related	1

VIRAGE-RB: PROPOSED PHASE 2/3 TRIAL DESIGN

Intravitreal (IVit) VCN-01 plus topotecan (VTOP) in refractory Rb

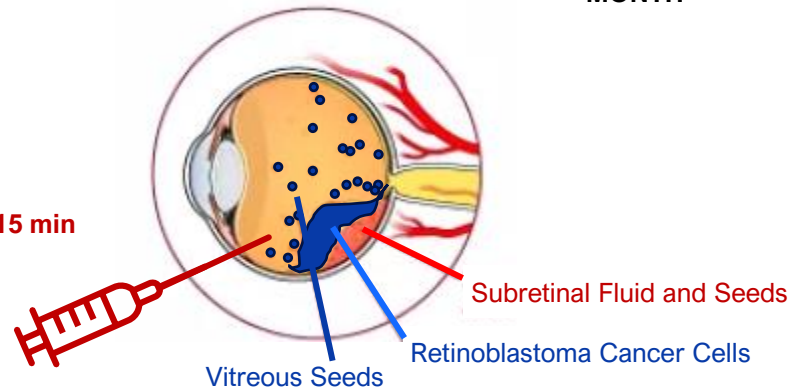


ENDPOINTS

- 1° Enucleation rate at 12 months
- Safety/tolerability
- 2° Event free survival
- Response rate
- Visual acuity

Exploratory endpoints liquid biopsy²

VTOP: IVit VCN-01 (2E10 vp) followed 15 min later by IVit topotecan (100 µg)



VIRAGE-RB PROPOSES PHASE 2/3 TRIAL TIMING

- Anticipate a single arm study with estimated N=25-30 patients¹
 - Global patient recruitment with treatment at 3-4 reference sites (US, Spain, India)
 - Budget ~\$12M (including manufacturing)
- Targeting potential approval before 30 Sep 2029
 - FDA, EMA submissions Q2-3 2026
 - First patient enrolment expected Dec 2026
 - Final data expected Q1 2029
 - Rolling BLA submission

THERIVA OV PIPELINE DISCOVERY AND DEVELOPMENT

Advancing founders' decades of world leading OV innovation

Common Features

Clinically-tested Adenovirus Expressing PH20
Hyaluronidase to **Degrade Tumor Stroma**

+

Additional Transgene Payloads to Enhance
Anti-tumor Immune Response and
Potentially Enable **Single-Agent** therapy

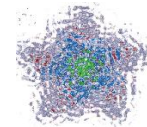
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Albumin Shield™ To Prevent Neutralization by
Anti-viral Antibodies and Facilitate IV Multidosing

Product Specific Features



VCN-01 Hyaluronidase alone



VCN-12 Hyaluronidase + Toxins



VCN-11 Hyaluronidase + Albumin Shield

MILESTONE SUMMARY





APPENDIX



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



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)



Vince Wachter PhD
SVP Corporate & Product
Development

Over 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

Advanced clinical development experience across oncology, infection, GI, metabolic diseases, transplantation, and drug delivery





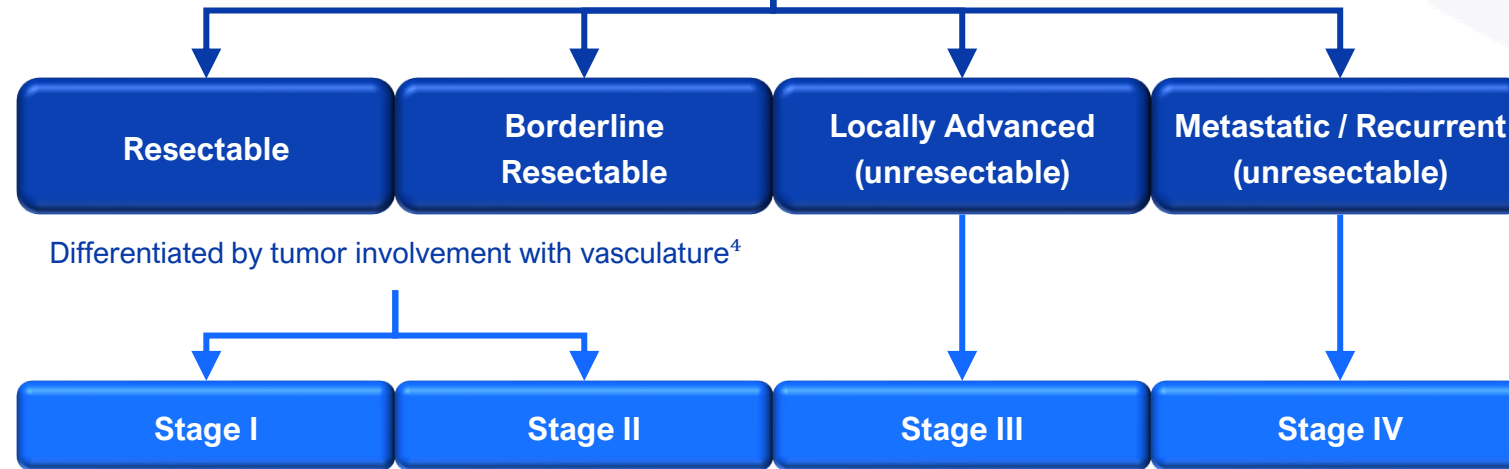
VCN-01 IN PANCREATIC CANCER

PANCREATIC CANCER STAGING

PDAC >90% pancreatic cancer¹; median age 67-68 yr; 51% male²
 1-year (5-year) overall survival 24% (9%)³; median 4-6 months²

Pancreatic Cancer

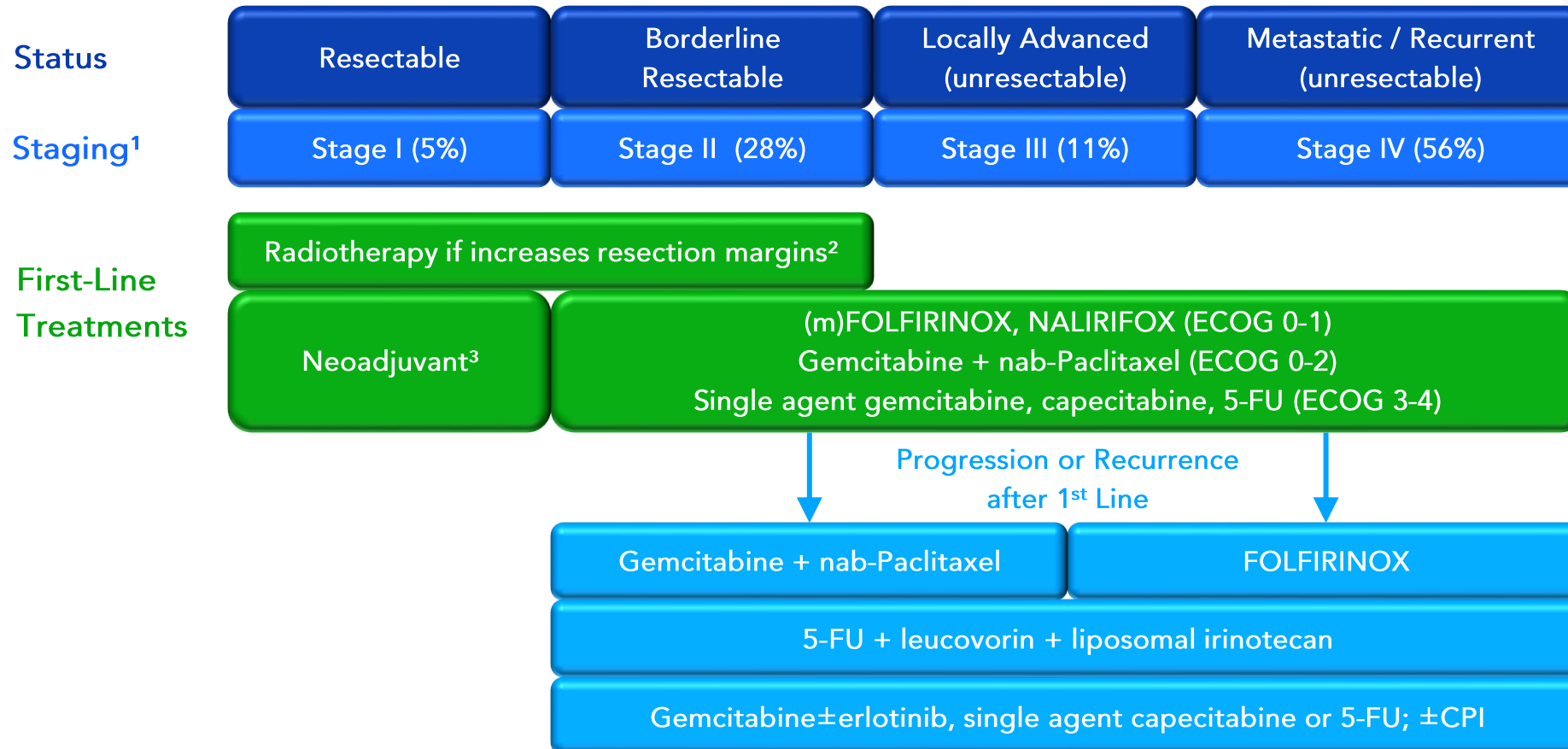
Male (per 100,000)³ N. America 9.3; W. Europe 9.9; E. Asia 7.0
 Female (per 100,000)³ N. America 6.9; W. Europe 7.4; E. Asia 4.8



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%											

¹PDAC 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. ²Bengtsson (2020) *Sci Rep* **10**:16425. ³GLOBOCAN 2020 survey of persons 0-74 years. Ushio (2021) *Diagnostics* **11**:562. ⁴Toesca (2018) *Int J Radiation Oncol Biol Phys* **100**:1155-1174. ⁵American Joint Committee on Cancer Tumor size, Nodal involvement, Metastasis. ⁶Yu (2015) *Gut* **64**:1783-9.

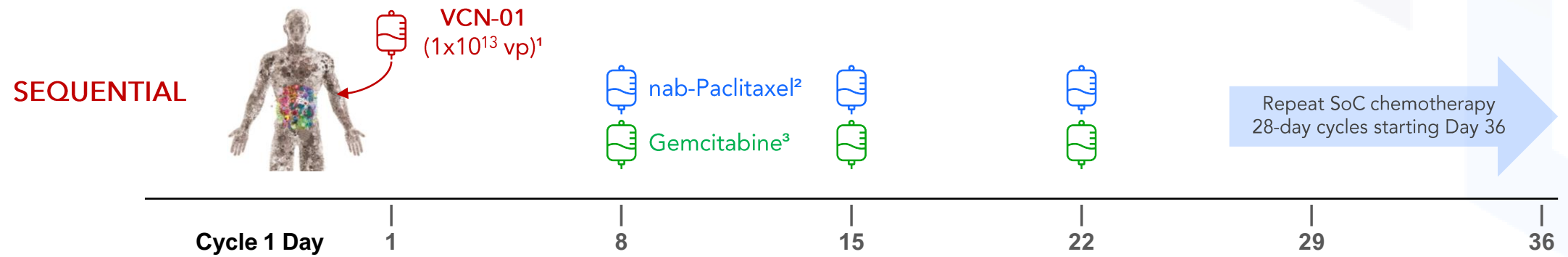
PANCREATIC CANCER CURRENT TREATMENTS



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

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

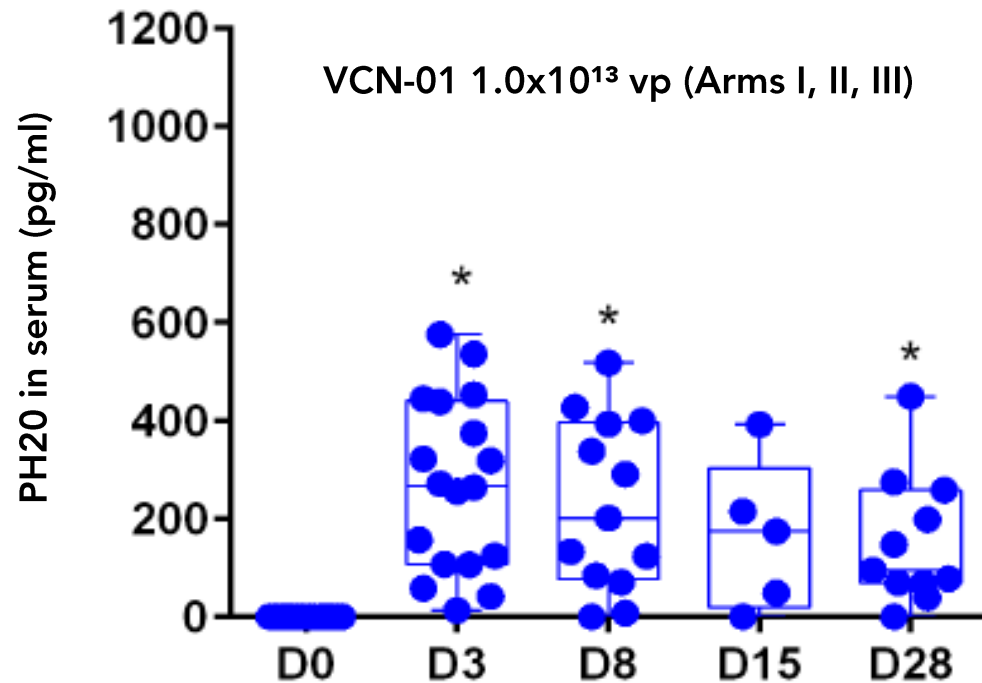
VCN-01 viral genomes and increased immune markers detected in tumor biopsies

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

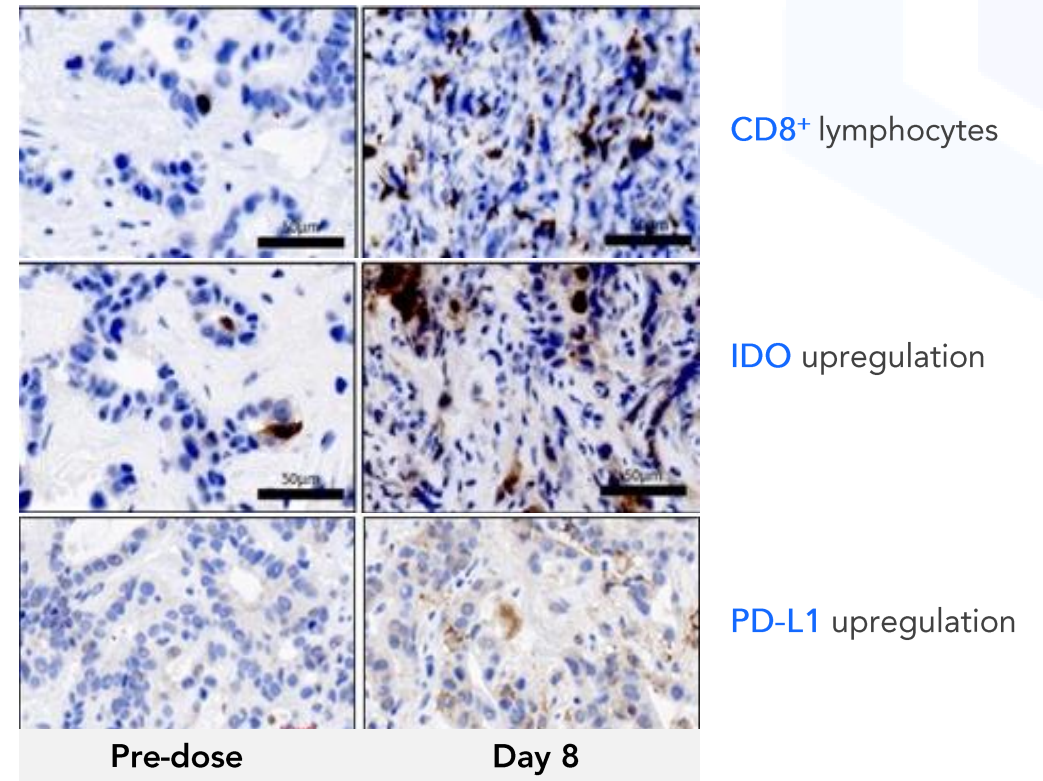
PHASE 1 DATA SUPPORT VCN-01 MODE-OF-ACTION

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

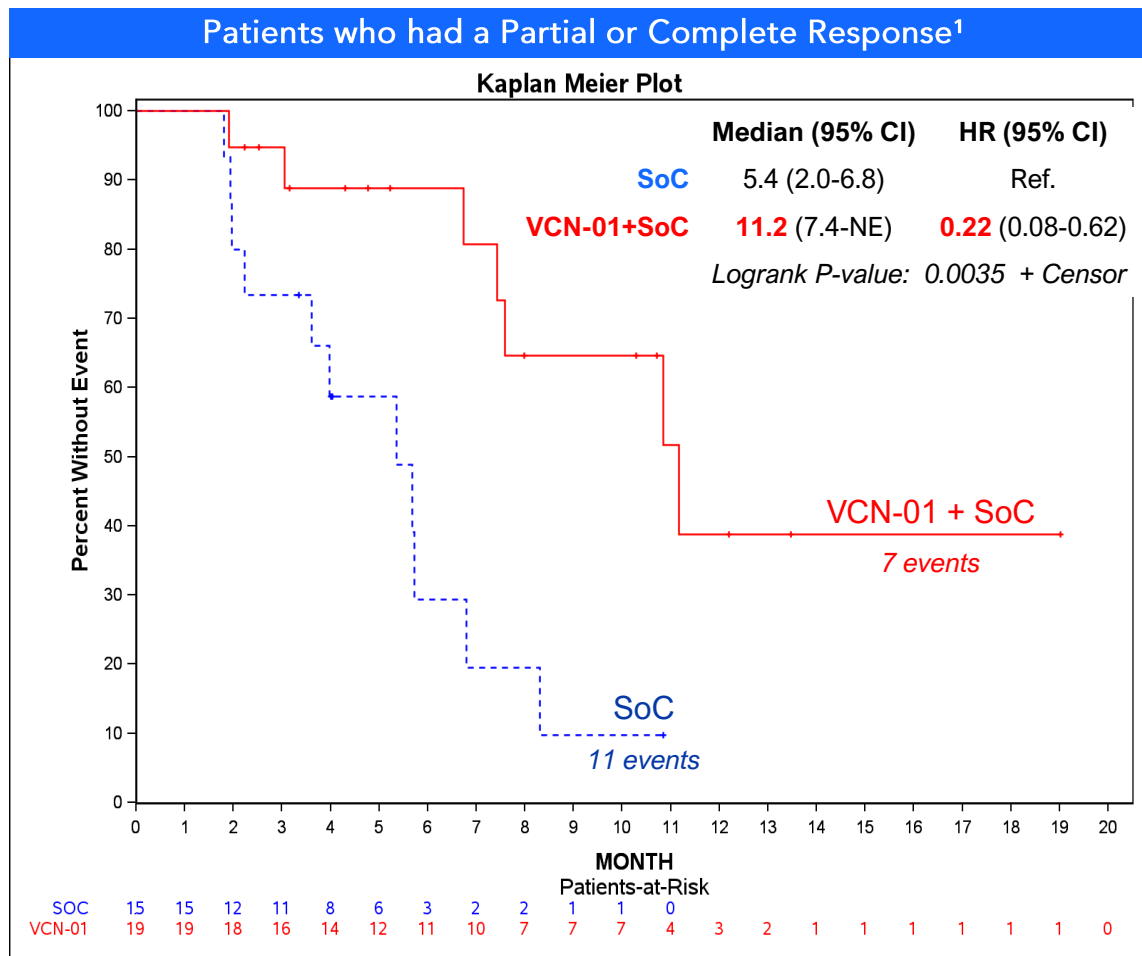


Immune markers upregulated in biopsies of **hepatic metastases***



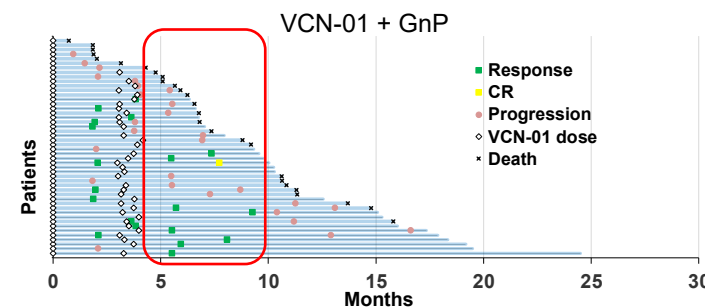
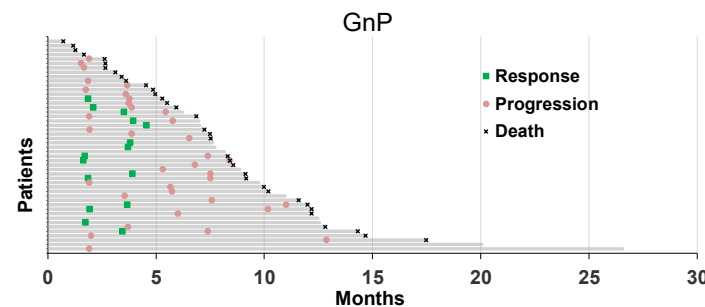
VIRAGE DATA SUPPORT IMMUNE MECHANISM-OF-ACTION

Long duration and late onset of responses



Objective Response Rates (ORR)¹

	Main Analysis (FAS) ¹		Subgroup (2 Doses VCN-01) ²	
	SoC	VCN-01 + SoC	SoC C4+	2*VCN-01 + SoC
N (%)				
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%)
		<i>p=0.314</i>		<i>p=0.533</i>



42% patients in VCN-01 + SoC exhibited late-emerging responses

¹According 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 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

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 NALIROX NAPOLI 3

Statistics		VIRAGE		NALIROX NAPOLI 3 ¹	
		VCN-01+Gem/Nab	Gem/Nab	NALIRIFOX	Gem/Nab
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	..



VCN-01 IN RETINOBLASTOMA



PH1 TRIAL DESIGN VCN-01 IN RB (HSJD-2015-RB TRIAL)

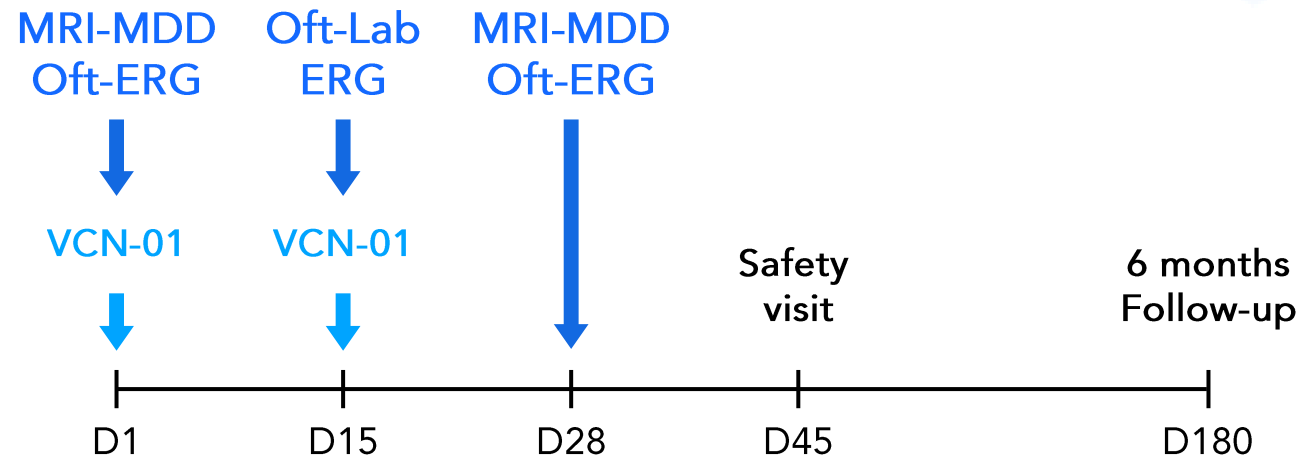


Investigator Sponsored Trial
PIs: Jaume Catalá, Guillermo Chantada

- Children (2-6 years)
- Intraocular retinoblastoma who failed conservative therapy and were facing imminent enucleation.
- Two intravitreal administrations 2 weeks apart
- Endpoints:
 - Safety profile
 - Antitumoral activity (delay of enucleation)

Dose escalation (monotherapy)

- 2E9 vp/eye 1 patient
- 2E10 vp/eye 8 patients



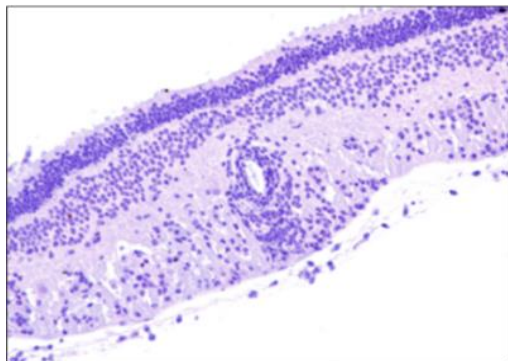
PHASE 1 TRIAL OF INTRAVITREAL VCN-01

DEMOGRAPHICS		Low dose 2E+9 vp/eye (n=1)	High dose 2E+10 vp/eye (n=8)
Age, years	Median (Range)	2	3.2 (2-7)
Sex (Male / Female)		0/1	5/3
Weight, Kg	Median (Range)	12	16.35 (9.4-31.0)
Height, cm	Median	98	103.5 (87-126)
RB1 gene mutation, n	Somatic	1	3
	Germinal	N/A	5
	<i>If germinal</i> With active tumor in ONLY one eye, and the contralateral eye already enucleated	N/A	5
IIRC Classification ¹	A Group	0	0
	B Group	0	1
	C Group	0	2
	D Group	1	5
	E Group	0	0

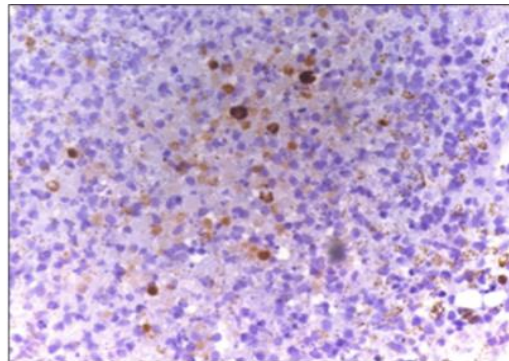
SAFETY DATA Ph1 TRIAL VCN-01 in RB:

Staining of VCN-01 viral proteins in healthy retina

Patient #1

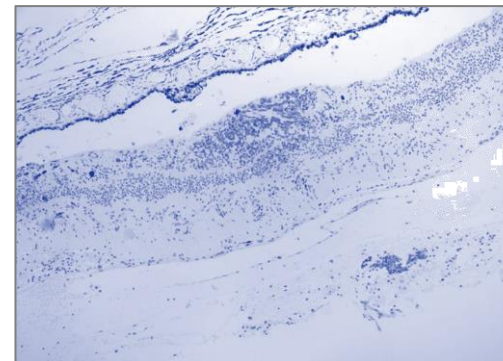


Conserved retina

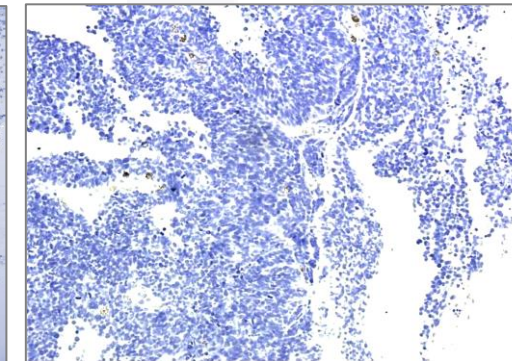


Calcified tumor area

Patient #8
(germline mutation)

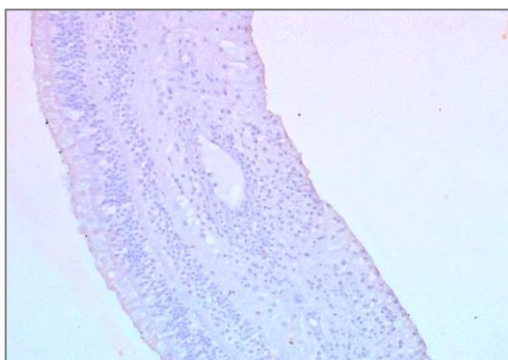


Conserved retina

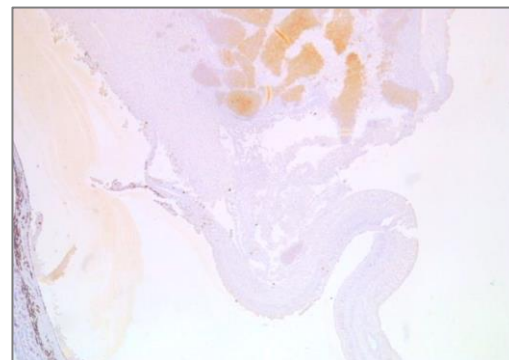


Tumor area

Patient #2
(germline mutation)

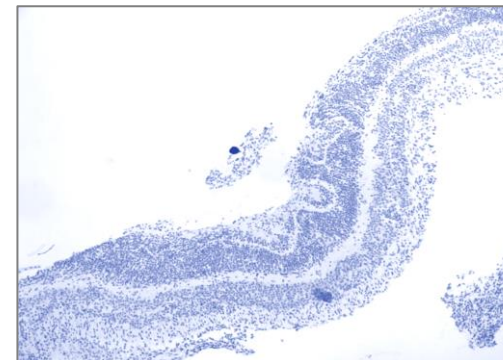


Conserved retina

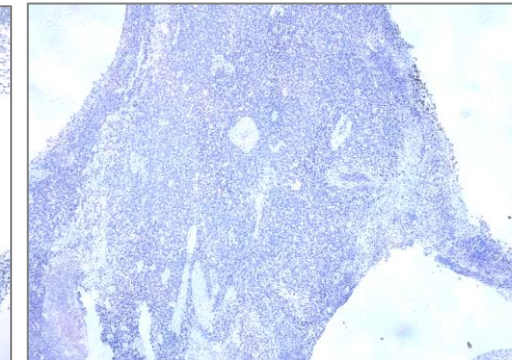


Calcified tumor area

Patient #9
(germline mutation)



Conserved retina

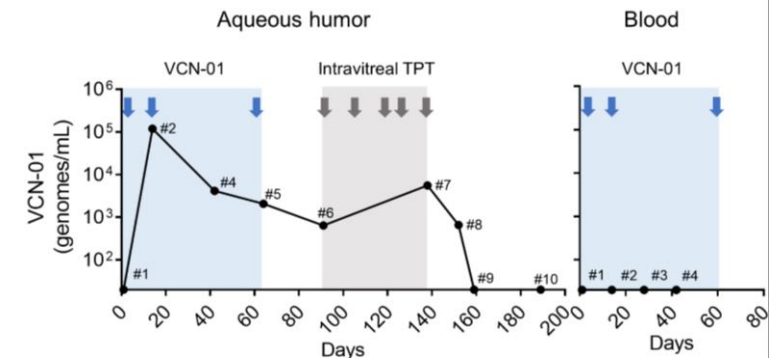
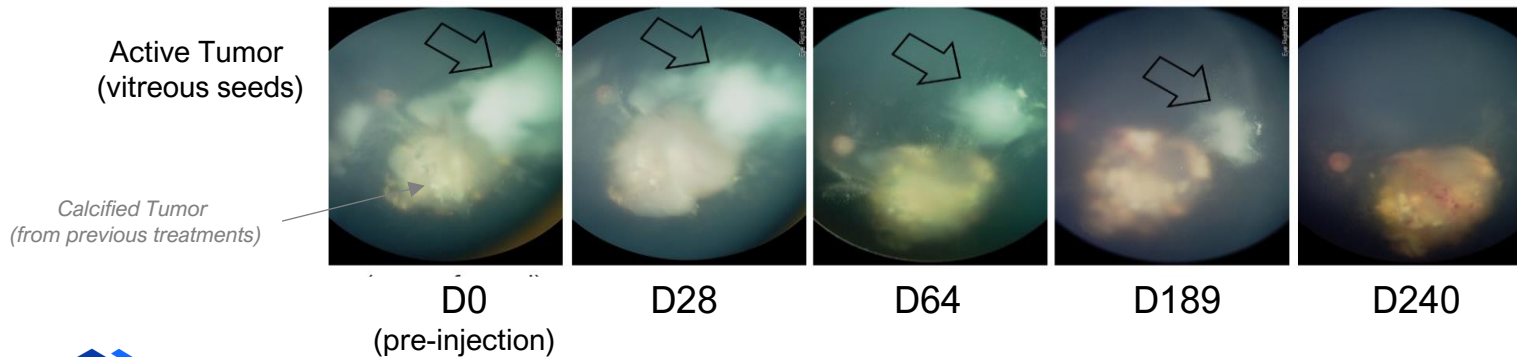
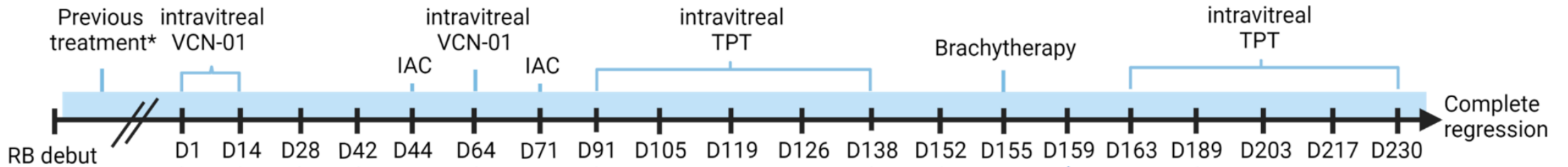


Tumor area

PRELIMINARY EVIDENCE OF ENHANCED ACTIVITY VCN-01 + TOPO-1 INH

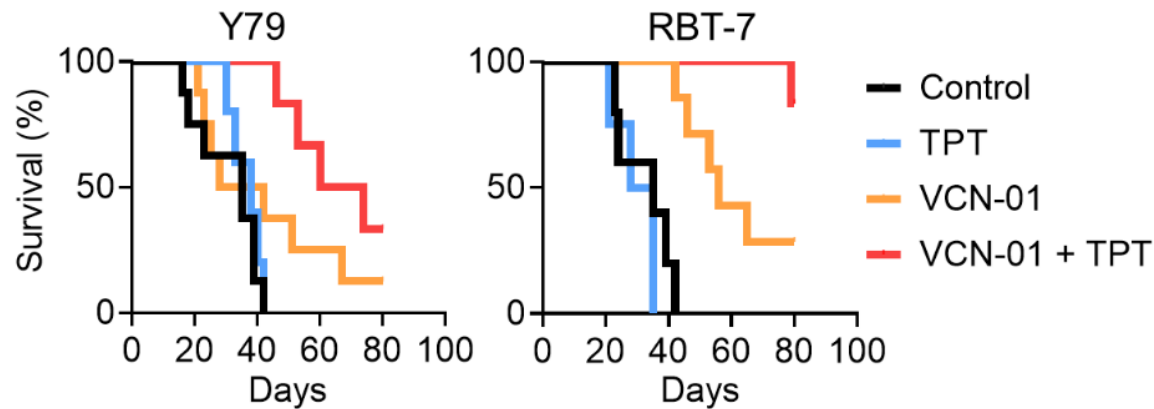
Patient #3

- 3-years old ♂
- Bilateral retinoblastoma (with germline Rb1 mutation), with 1st eye already enucleated.
- Previous treatments:
 - Systemic chemotherapy CBP/VP-16/VCR (followed by intraarterial dosing of topotecan/melphalan).
 - Tumor relapse 9 months later → Intravitreal melphalan: NO RESPONSE.

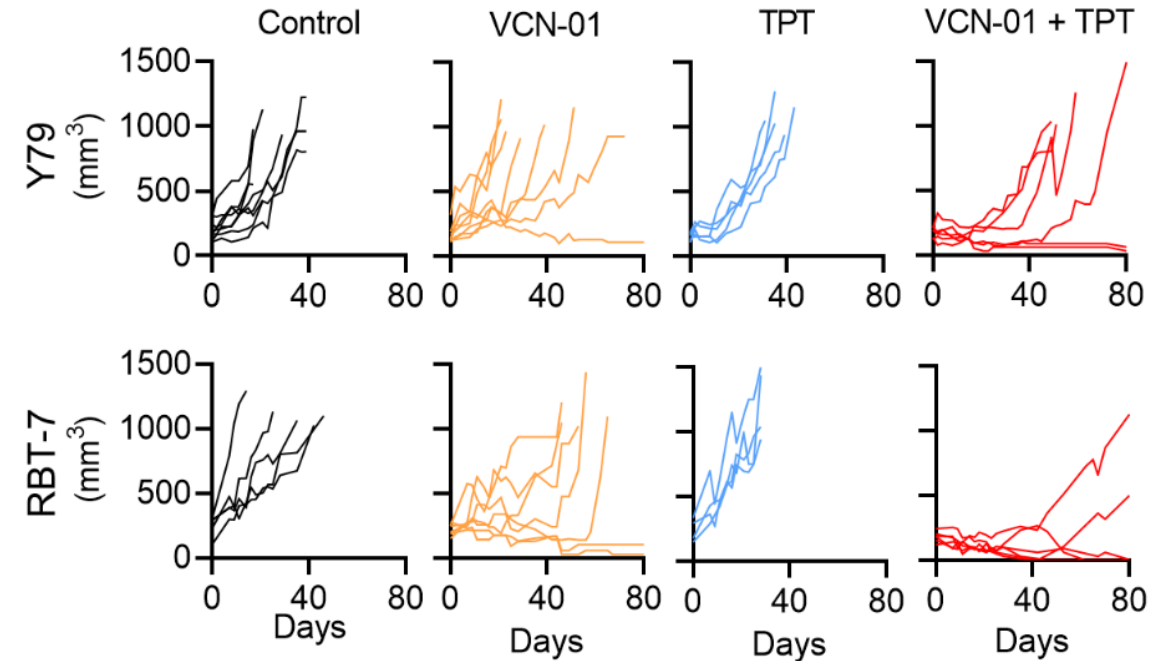


TOPO-1 INHIBITORS ENHANCE VCN-01 ANTITUMOR ACTIVITY

Improved ocular survival after intravitreal VCN-01 and Topotecan in intraocular RB



Ocular Survival	Y79 model	RBT-7 model
Control	35 days	35 days
VCN-01 + TPT	67 days	80 days
<i>p</i> -value	0.0009	0.0021



Two intratumoral (intravitreal) injections of VCN-01 in the left eye in s.c. xenografts, subsequent treatment with 6 cycles of systemic topotecan



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