Corporate Overview

November 2023

Theriva BIOLOGICS

FORWARD LOOKING STATEMENTS

This presentation includes 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 potential of VCN-01, VCN-11, VCN-12 and Theriva OVs and their ability to overcome key OV challenges; clinical advancement of VCN-01 (including completion of enrollment into the pancreatic ductal adenocarcinoma [PDAC] Phase 2 clinical trial in H1 2024; potential expansion of VCN-01 use in different lines of PDAC treatment; potential synergistic antitumor effects of VCN-01 with topoisomerase inhibitors; the potential of VCN-01 to enable immuno-oncology therapies in refractory tumors; initiation of a Company sponsored retinoblastoma [Rb] clinical trial); the potential of the albumin shield to enhance OV systemic delivery; and obtaining data from Cohort 2 of the SYN-004 Phase 1b/2a clinical trial in allogeneic hematopoietic cell transplant (HCT) patients in H1 2024. These forward-looking statements are based on management's expectations and assumptions as of the date of this press release and are subject to a number of risks and uncertainties, many of which are difficult to predict that could cause actual results to differ materially from current expectations and assumptions from those set forth or implied by any forward-looking statements. Important factors that could cause actual results to differ materially from current expectations include, among others, Theriva Biologics' product candidates demonstrating safety and effectiveness, as well as results that are consistent with prior results, the ability to initiate and complete clinical trials on time and achieve the desired results and benefits, continuing clinical trial enrollment as expected, the ability to obtain regulatory approval for commercialization of product candidates or to comply with ongoing regulatory requirements, regulatory limitations relating to Theriva Biologics' 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 Theriva Biologics' products, developments by competitors that render such products obsolete or non-competitive, Theriva Biologics' ability to maintain license agreements, the continued maintenance and growth of Theriva Biologics' patent estate, the ability to continue to remain well financed, and other factors described in Theriva Biologics' Annual Report on Form 10-K for the year ended December 31, 2022 and its other filings with the SEC, including subsequent periodic reports on Forms 10-Q and 8-K. The information in this presentation 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 is undergoing a Phase 2b clinical trial in first-line metastatic pancreatic cancer in combination with SoC chemotherapy
- VCN-01 Phase 1 clinical trials support multiple additional indications (retinoblastoma, HNSCC, CRC) and combinations (immunotherapies)
- Albumin Shield™ platform and innovative oncolytic virus discovery engine enable development of a distinct product pipeline

Financial Snapshot	
Exchange	NYSE American
Ticker	TOVX
Cash (6/30/2023)	$34.2M
Projected cash runway	Q4 2024
Average Daily Volume (3M Ave)	50.5K
Locations	Rockville, MD Barcelona, Spain

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CRC colorectal cancer. HNSCC head and neck squamous cell carcinoma. SoC standard of care. Immunotherapies include immune checkpoint inhibitors and CAR-T cells.

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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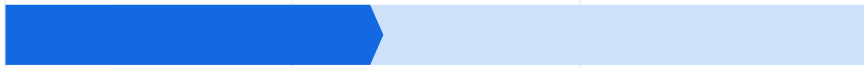
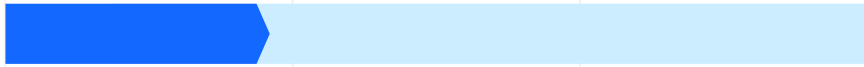
THERIVA PIPELINE

Candidate	Target	Pre-IND / Phase 1 / Phase 2	Collaborators	Status*
VCN-01 Selective, Stroma Degrading OV	Pancreatic Cancer (IV) with gemcitabine/nab-paclitaxel			Phase 2 Study On-going (ODD EU, US)
	Retinoblastoma (IVit)		Sant Joan de Déu Hospital Materno-Infantil Universitat de Barcelona	Phase1 Study On-going (ODD US)
	HNSCC (IV) + durvalumab		ICO Institut Català d'Oncologia	Phase 1 Treatment Complete Survival Follow-up On-going
	Solid Tumors – Brain, Ovarian, PDAC (IV)		LEEDS; University of Pennsylvania	Phase 1 Studies On-going
VCN-11 Albumin Shield OV	Solid tumors (IV)		ICO Institut Català d'C; IDIBELL	Preclinical Studies On-going
SYN-004 [1,2] Oral β-lactamase	**Prevention of aGVHD in allo-HCT**		Washington University in St. Louis	Phase 1b/2a On-going
SYN-020 [3] Oral IAP	**Potential indications include NAFLD/NASH, celiac, radiation enteritis**		Massachusetts General Hospital	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. IAP recombinant bovine intestinal alkaline phosphatase. HNSCC head and neck squamous cell carcinoma. IV intravenous. IVit intravitreal. MAD multiple ascending dose. ODD Orphan Drug Designation.

VCN-01 IS A UNIQUELY ENGINEERED HUMAN ADENOVIRUS 5

Systemic

Access primary and metastatic lesions
High dose, highly replicating

Selective

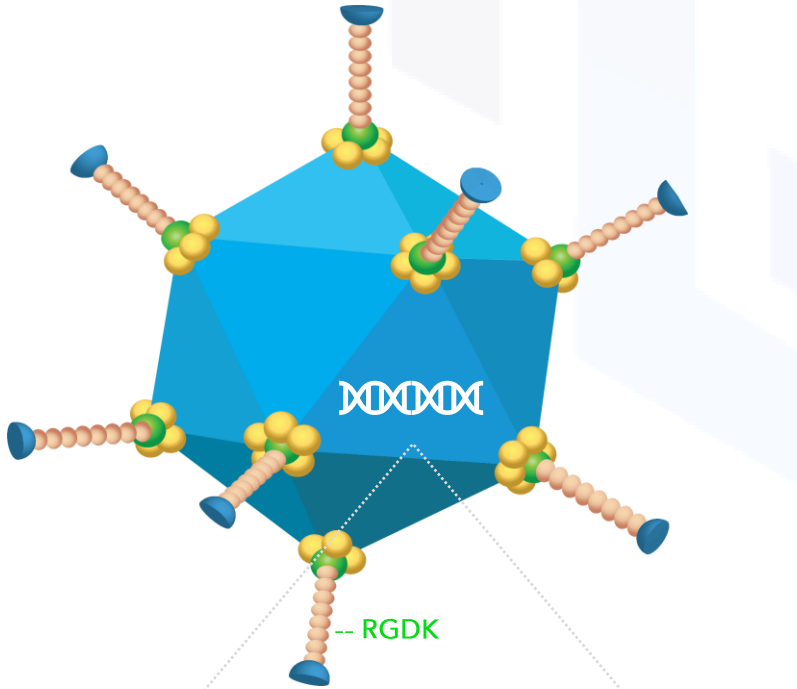
Replicates only in tumor cells
Liver detargeted

Stroma Degrading

Expresses PH20 (hyaluronidase) after viral replication cycle

Self Reporting

PH20 in blood is a biomarker for virus replication in tumors



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

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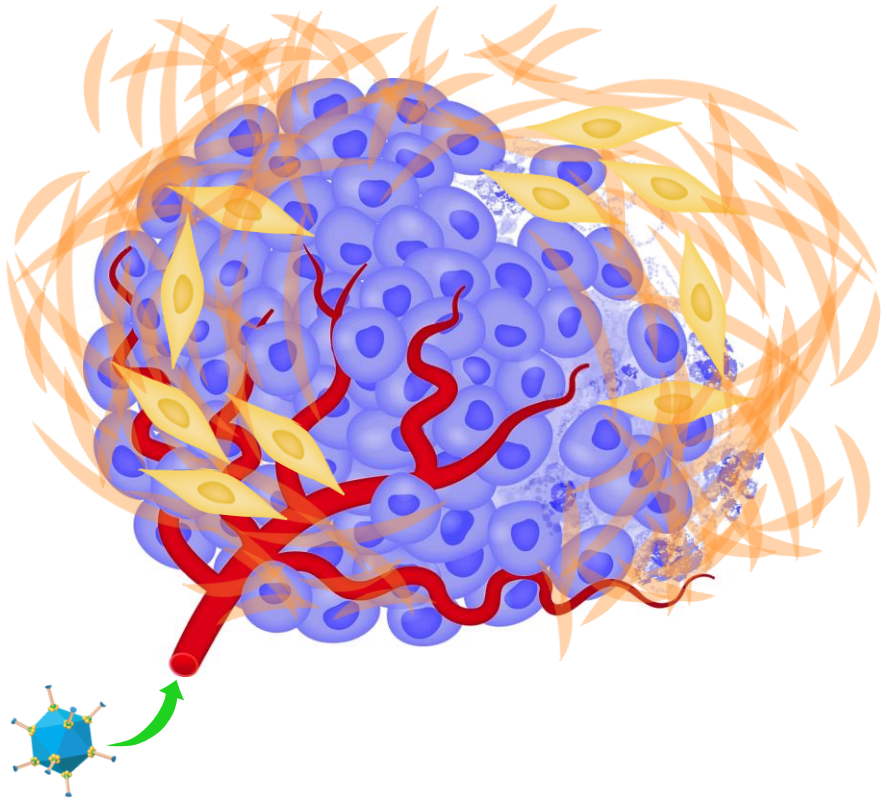
Replication enhanced by significantly increased E2F binding. E1a-Δ24 gene deletion means replication only in cells with a defective Rb-E2F pathway. Fiber shaft RGDK modification. PH20 soluble human testicular hyaluronidase enzyme expression is under control of the virus major late promoter (MLP).

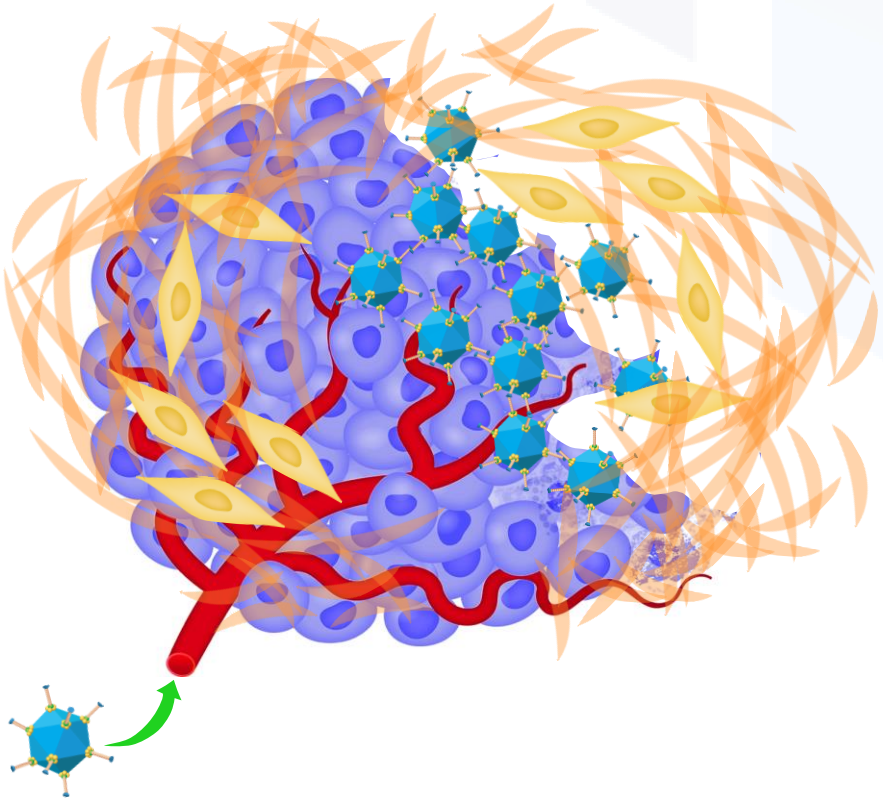
VCN-01 DESIGNED TO HAVE MULTIPLE ANTI-TUMOR ACTIONS

Tumor Surrounded by STROMA



VCN-01

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



VCN-01

Stroma

Cancer Associated Fibroblast

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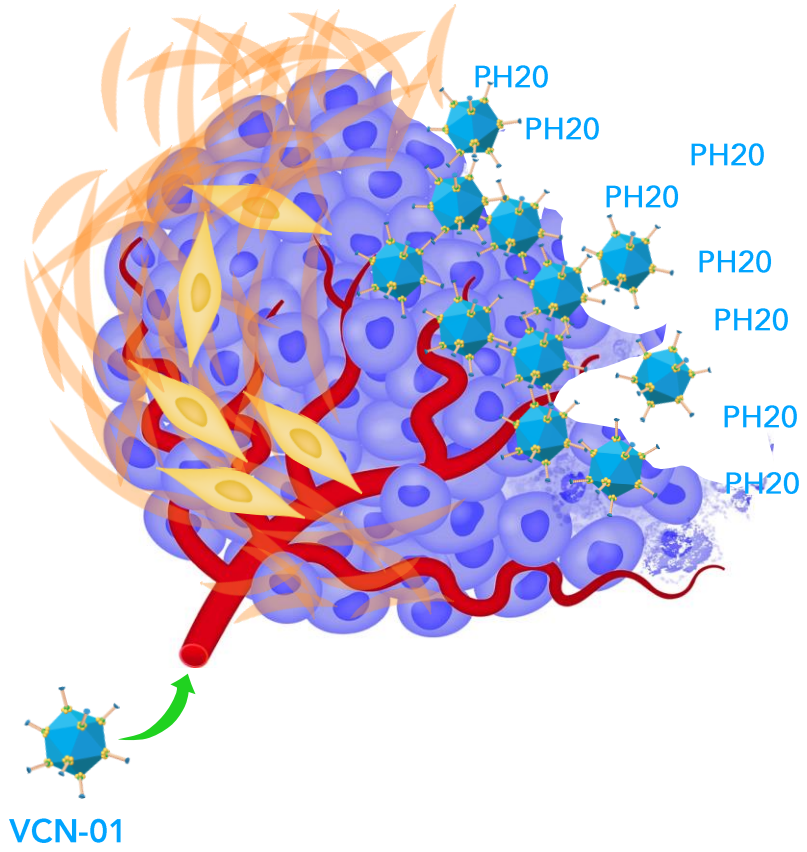
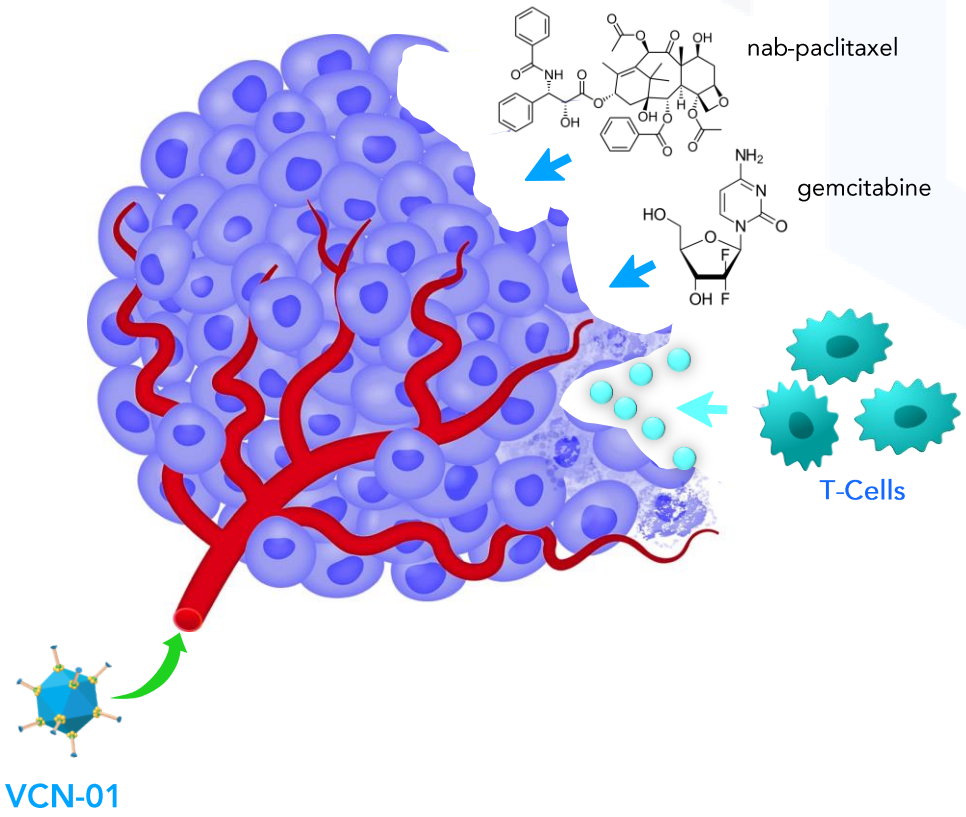
VCN-01 DESIGNED TO HAVE MULTIPLE ANTI-TUMOR ACTIONS

2 **STROMA DEGRADATION** by PH20 facilitates tumor access and killing by coadministered cancer therapies



3 **COMBINED EFFECTS** increase tumor immunogenicity and elicit an anti-tumor immune response



Stroma

Cancer Associated Fibroblast

Neoantigen

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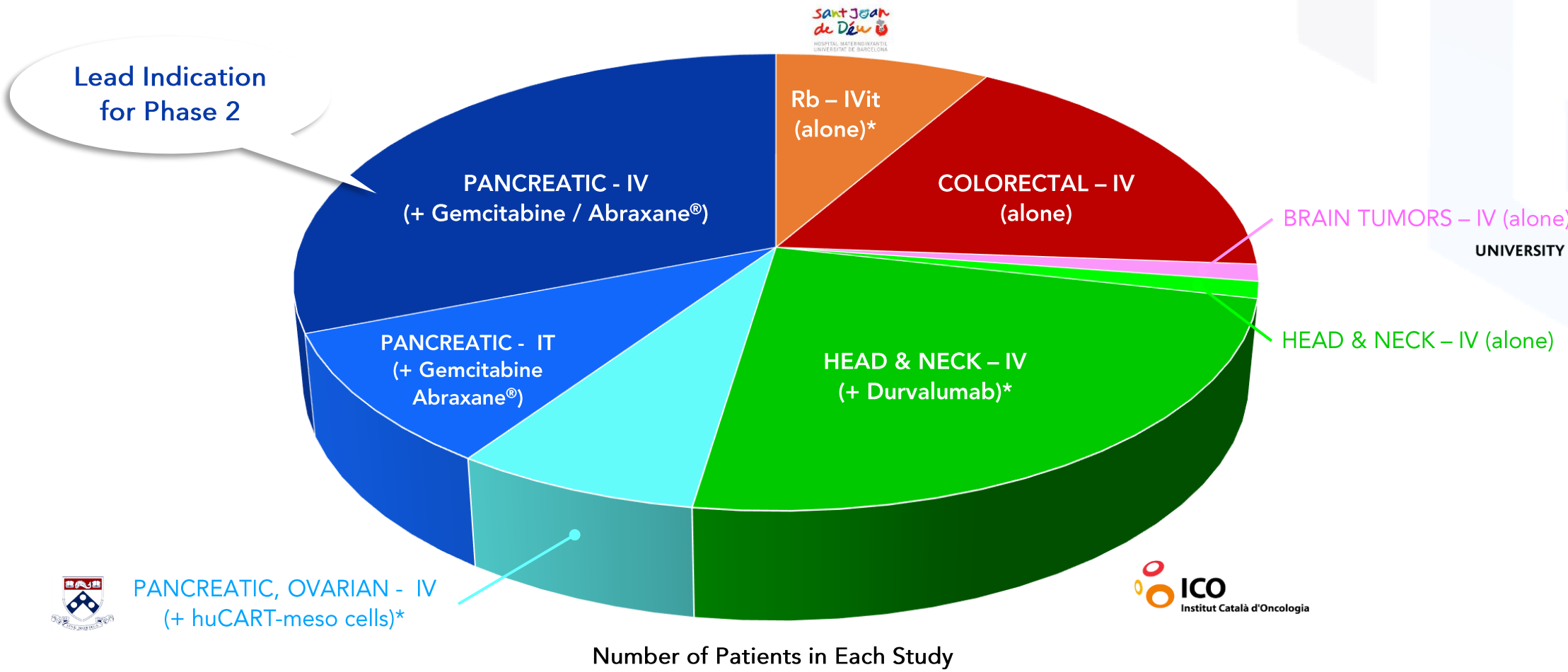
VCN-01 EXTENSIVE PHASE 1 PROGRAM

84 patients treated in multiple indications and combinations



*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.

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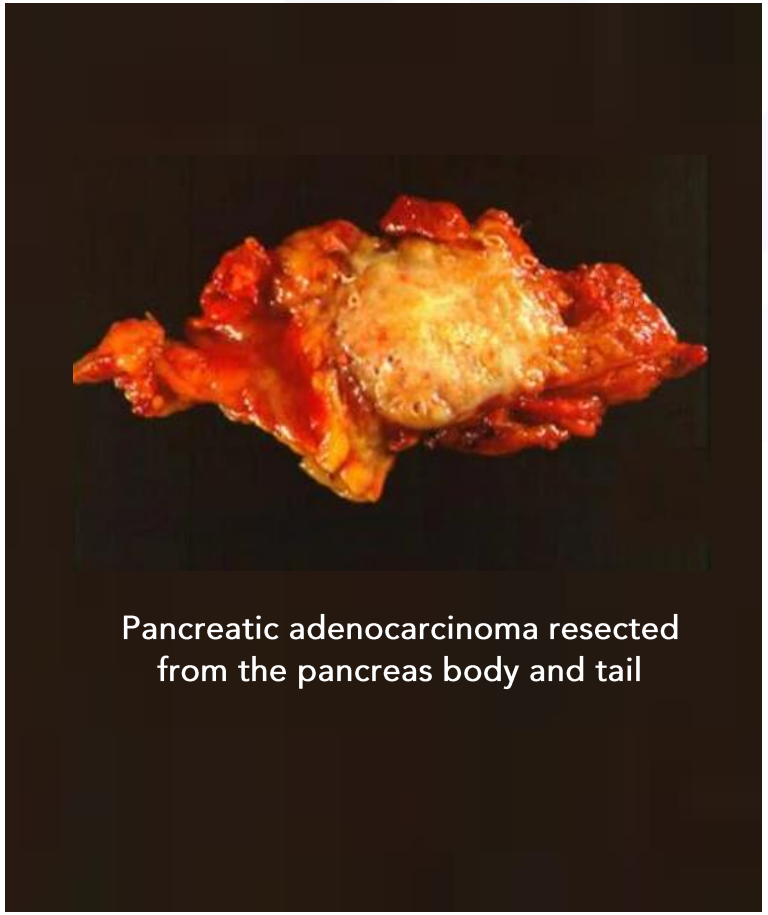
VCN-01 PHASE 2 PROGRAM IN PANCREATIC CANCER

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[1]
  - USA est. 62,210 new cases and 49,830 deaths in 2022[2,3]
- 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
  - Estimated treatment market ~$2.5B (2022) ~$7.0B (2030)[5]



Pancreatic adenocarcinoma resected from the pancreas body and tail

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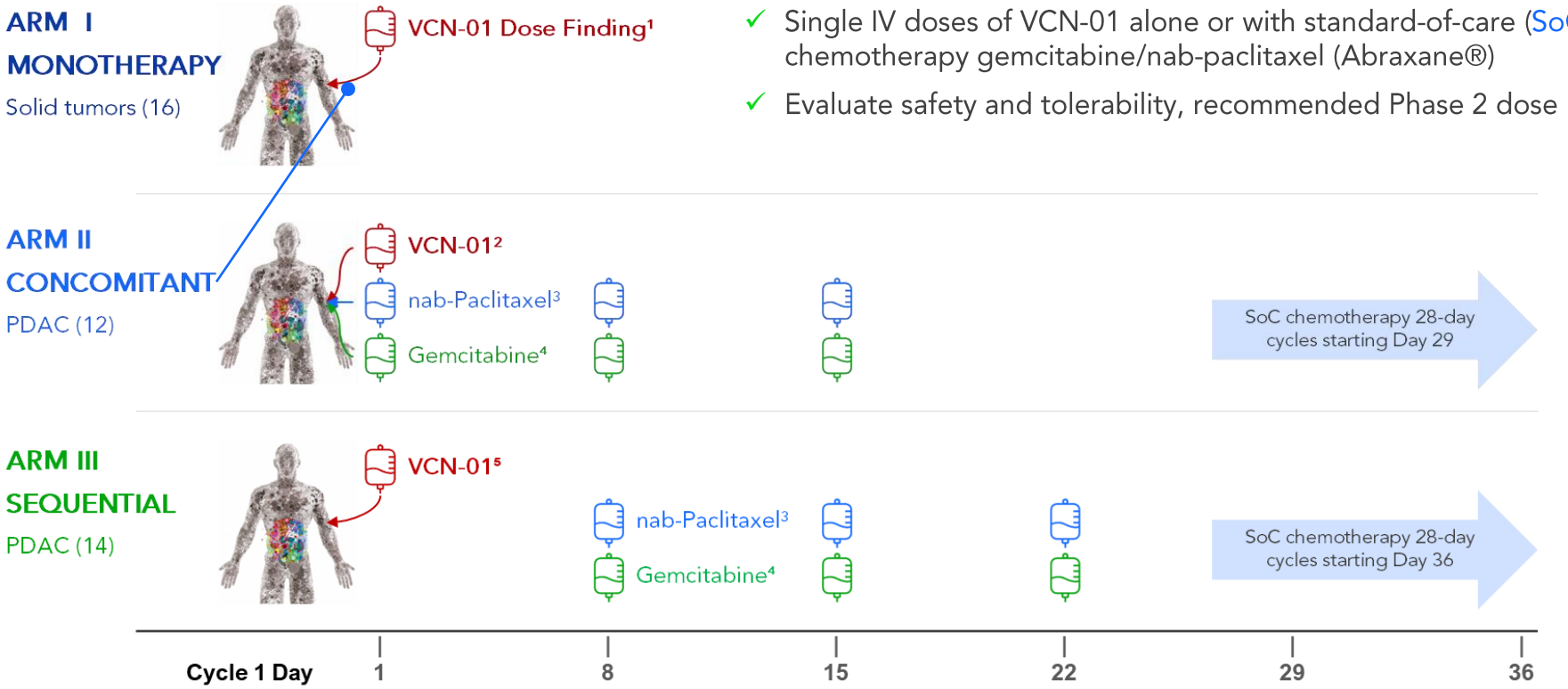
[1]Michael (2019) BMC Palliat Care 18:13, Bengtsson (2020) Sci Rep 10:16425, Carioli (2021) Ann Oncol 32:478, ASCO Pancreatic Cancer Statistics. [2]SEER Cancer Stat Facts: Pancreatic Cancer website. [3]WW estimated 495,773 new cases and 466,003 deaths in 2020; Sung (2021) CA Cancer J Clin 71:209. [4]Tahkola (2021) Sci Rep 11:12216, Placencio-Hickok (2022) Pancreatology 22:92. [5]Data Bridge Market Research website.

VCN-01 FAVORABLE OUTCOMES IN PHASE 1 TRIAL

Multicenter, open-label, dose escalation study [NCT02045602]



- ✓ 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

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[1]Single dose of VCN-01 ($1x10^{11}$ to $1x10^{13}$ vp/dose) administered by 10 min IV infusion. [2]VCN-01 doses $3.3x10^{12}$ vp (n=6) and $1x10^{13}$ vp (6). [3]nab-Paclitaxel (Abraxane®; 30 min infusion) administered at least 4 hours after VCN-01. [4]Gemcitabine (30 min infusion) administered immediately after Abraxane® infusion. [5]VCN-01 doses $3.3x10^{12}$ vp (8) $1x10^{13}$ vp (6). Garcia-Carbonero (2022) J Immunother Cancer 10:e003255.

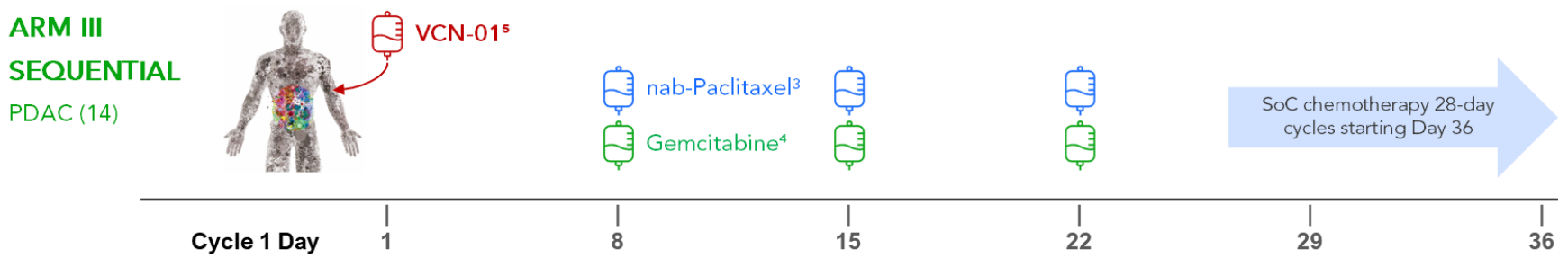
VCN-01 FAVORABLE OUTCOMES IN PHASE 1 TRIAL

Multicenter, open-label, dose escalation study [NCT02045602]

OUTCOME	VCN-01 DOSE, virus particles (n)[1]			SoC ALONE[2]
Sequential Regimen	$3.3x10^{12}$ (6)	$1.0x10^{13}$ (6)	Combined (12)	Phase 3 (431)
Responders, %	16.7%	83.3%	50.0%	22.9%
Median OS, months	13.1	20.8	13.5	8.5
Median PFS, months	9.9	6.7	7.2	5.5
Survival ≥12 months	.	.	67%	35%
Survival ≥24 months	.	.	25%	16%

KOLs advise that OS ≥15 months is a significant patient outcome

RELATED AEs IN ≥1 PATIENT[1]	CTCAE SEVERITY	
VCN-01 Combined, Sequential Regimen	Grade 1-2	Grade ≥3
Pyrexia/Influenza-like Illness	12 (85.7%)	-
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%)	-

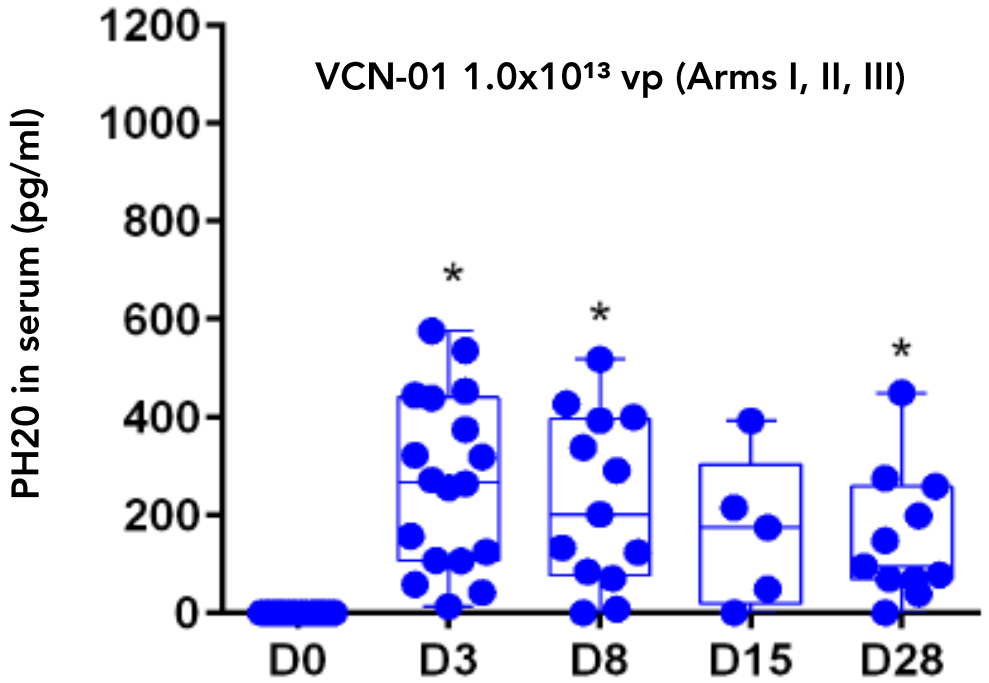


[1]Single dose of VCN-01 ($1x10^{11}$ to $1x10^{13}$ vp/dose) administered by 10 min IV infusion. [2]VCN-01 doses $3.3x10^{12}$ vp (n=6) and $1x10^{13}$ vp (6). [3]nab-Paclitaxel (Abraxane®; 30 min infusion) administered at least 4 hours after VCN-01. [4]Gemcitabine (30 min infusion) administered immediately after Abraxane® infusion. [5]VCN-01 doses $3.3x10^{12}$ vp (8) $1x10^{13}$ vp (6). Garcia-Carbonero (2022) J Immunother Cancer 10:e003255.

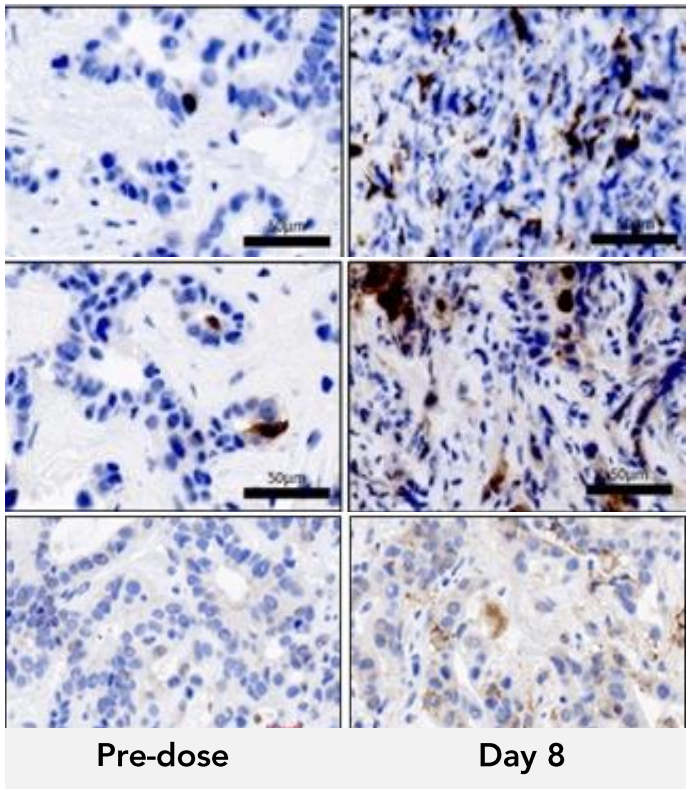
PHASE 1 DATA SUPPORT VCN-01 MODE-OF-ACTION

Remodels the tumor matrix and turns "cold" tumors "hot"

Built-in biomarker: PH20 levels in patient sera indicate sustained VCN-01 activity in tumors



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



CD8⁺ lymphocytes

IDO upregulation

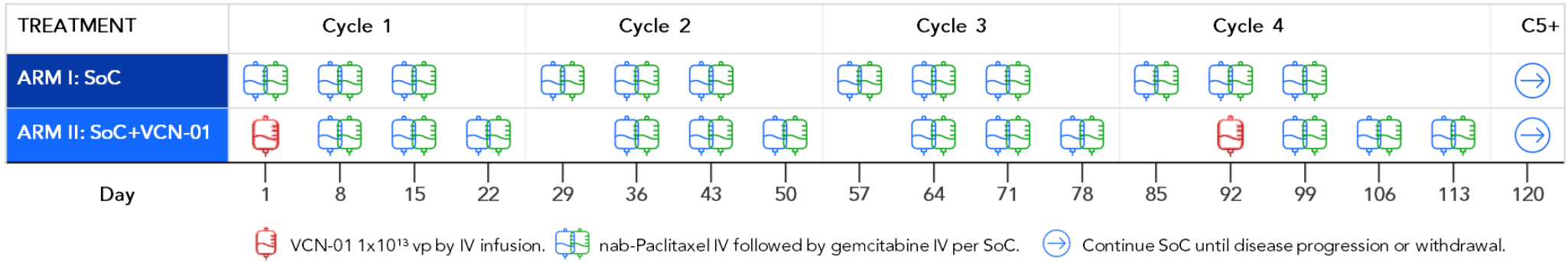
PD-L1 upregulation

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.

VIRAGE PHASE 2B CLINICAL TRIAL in PDAC

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

- Study on-going in patients with first-line metastatic pancreatic ductal adenocarcinoma (PDAC)
- Up to 92 patients to be enrolled at sites in Spain and the USA (complete enrollment expected H1 2024)
- 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



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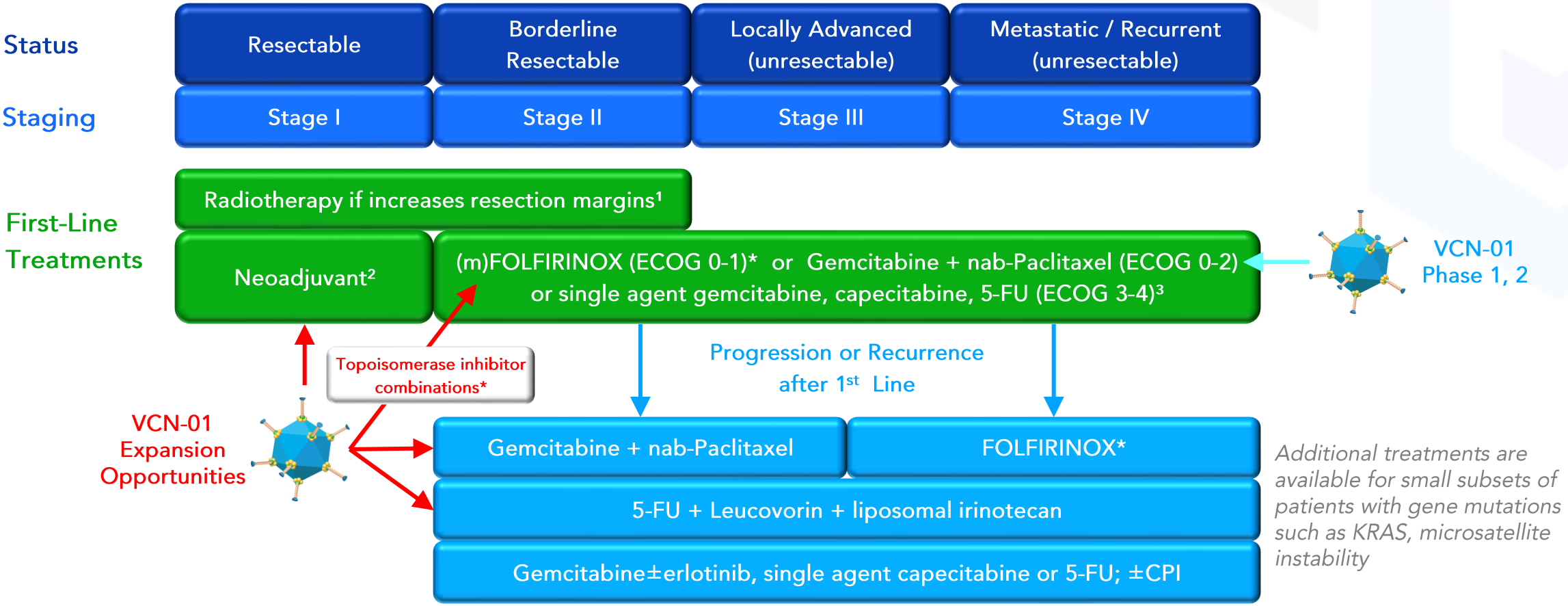
SoC standard of care

EXPANSION OPPORTUNITIES for VCN-01 in PDAC

Alternate treatment lines and new chemotherapy combinations



Additional treatments are available for small subsets of patients with gene mutations such as KRAS, microsatellite instability

[1]Used in <20% of PDAC cases. [2]Identical to first-line chemotherapy. [3]Eastern Cooperative Oncology Group Performance Status.
Abbreviations: CPI checkpoint inhibitor. (m)FOLFIRINOX (modified) leucovorin+5-FU+irinotecan+oxaliplatin. nab-Paclitaxel nanoparticle albumin-bound paclitaxel. *NALIRIFOX leucovorin+ 5-FU+liposomal irinotecan+oxaliplatin regimen sNDA accepted by FDA June 2023 for first line metastatic PDAC.
Adapted from Tempero (2021) *J Natl Compr Canc Netw* **19**:439.

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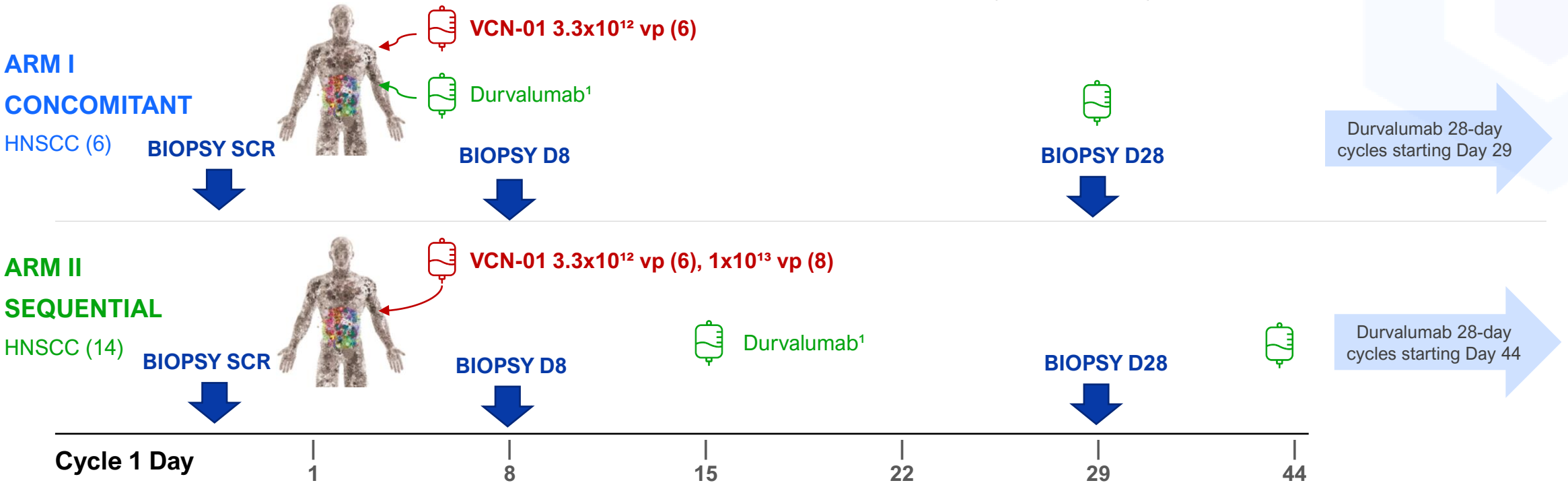
VCN-01 + IMMUNE CPI
PHASE 1 DATA IN R/M HNSCC

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



[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

VCN-01 FINDINGS in R/M HNSCC

Data support VCN-01 MOA and immune enhancing effects

- ✓ VCN-01 has an acceptable safety 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 (including one complete response)

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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.

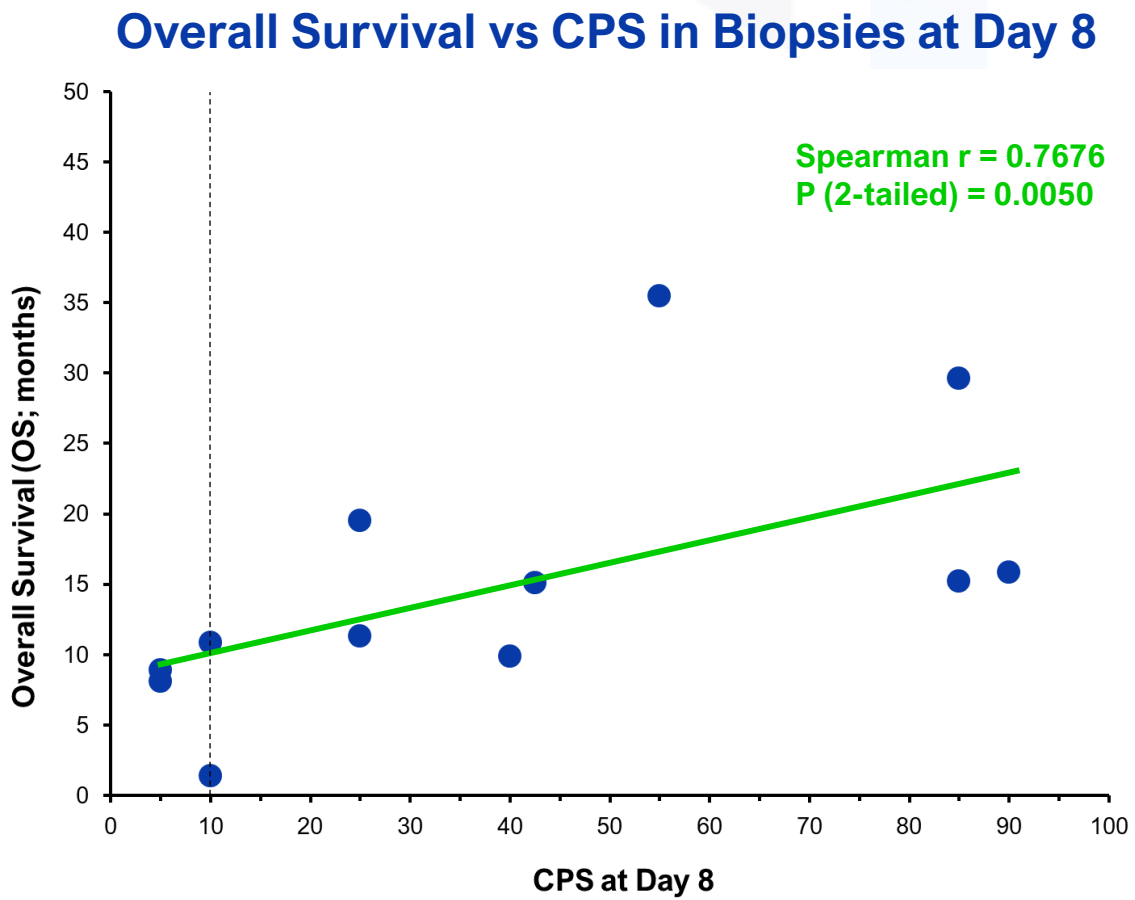
EXTENDED SURVIVAL with VCN-01+DURVALUMAB

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)
- Significant correlation of survival with CPS 8-days after VCN-01 treatment



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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

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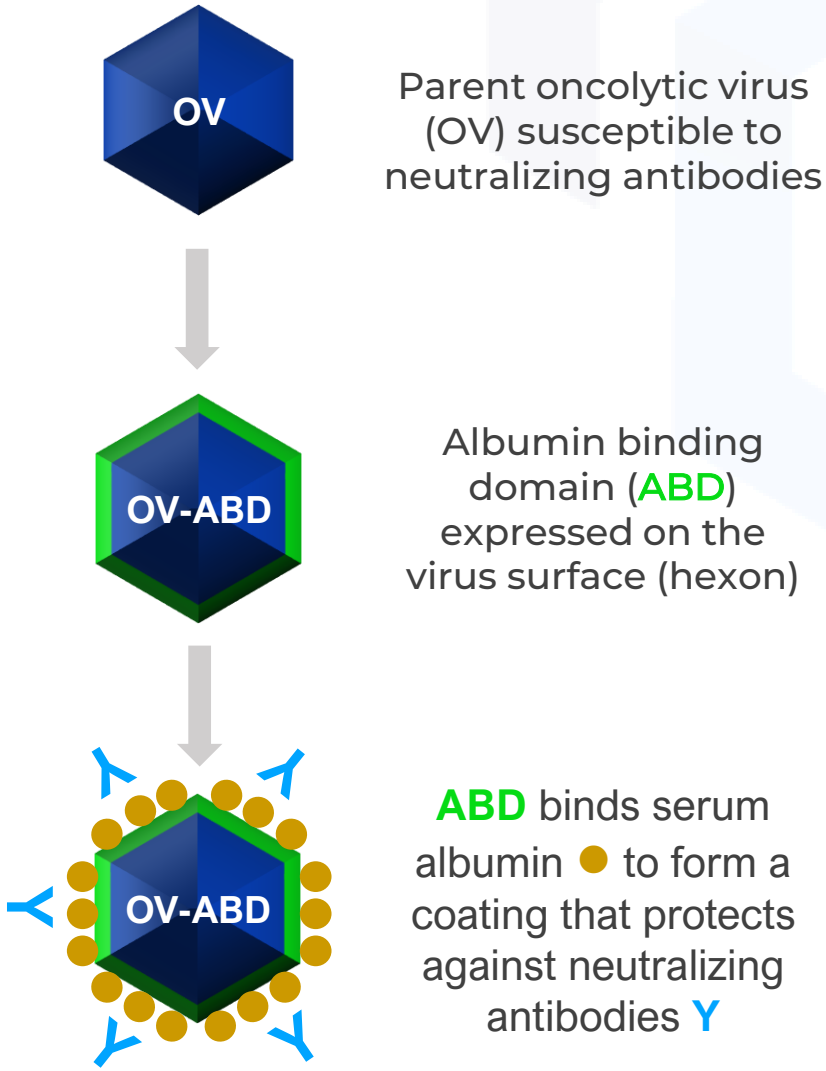
NEXT GENERATION OV DISCOVERY PLATFORM

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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[1]Rojas (2016) J Control Rel 237:78; ABD binds mouse and human serum albumin, but not bovine; [2]Mato-Berciano (2021) J Control Rel 332:517.

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

+

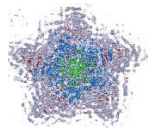
Albumin Shield™ To Prevent Neutralization by anti-viral Antibodies and Facilitate IV Multidosing

+

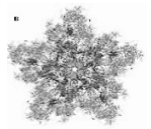
Unique Multifunctional Proteins to Turn Cold Tumors Hot and Enhance Anti-tumor Immune Response

Product Specific Features

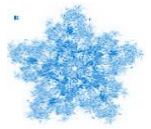
VCN-11 Hyaluronidase alone



VCN-12 Hyaluronidase + Toxins



VCN-13 Fusion Hyaluronidase + scPD-L1



VCN-XX Hyaluronidase + other payloads

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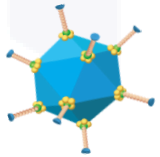
SUMMARY

THERIVA OV PORTFOLIO HIGHLIGHTS

Multiple modes of action, indications, and combinations



- Highly differentiated OV designed to have multiple antitumor effects
  - Systemic administration, selective tumor replication, stroma degradation
  - Designed to increases cell lysis, tumor immunogenicity, and tumor access by co-administered therapies
- Multiple potential value opportunities for lead product VCN-01
  - Phase 2b study in an orphan clinical indication with high unmet medical need (PDAC)
  - Phase 1 clinical data support evaluation in additional cancers (HNSCC, Rb)
  - Phase 1 clinical data suggest potential to enable use of CPIs in refractory patients
  - Phase 1 study evaluating the potential to facilitate CAR-T cell treatment of solid tumors
  - Preclinical data indicate antitumor synergy for VCN-01 in combination with topoisomerase inhibitors
- 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. PDAC pancreatic ductal adenocarcinoma. R/M HNSCC refractory/metastatic head and neck squamous cell carcinoma. SoC standard of care (gemcitabine + nab-paclitaxel in PDAC). Alternate indications include retinoblastoma and brain tumors; phase 1 data support additional evaluation in colorectal cancer. Topoisomerase inhibitors include topotecan and irinotecan.

PROJECTED MILESTONES AND NEWS FLOW

Q2 2023

- VCN-01 PDAC Orphan Drug Designation USA

Q3 2023

- VCN-01 PDAC Phase 2 1st patients dosed USA

Q4 2024

- VCN-01 HNSCC ISS survival/efficacy data
- VCN-01 FDA meeting retinoblastoma program

H1 2024

- VCN-01 PDAC Phase 2 enrollment complete
- VCN-12 candidate selection[2,3]
- SYN-004 Phase 1b/2a data 2nd cohort

Theriva BIOLOGICS

[1]Contingent on appropriate funding and VCN-01 clinical trials progress. [2]VCN-12 is an armed version of VCN-11 designed to express an additional functional payload.[3]VCN-11 is the first clinical candidate using the Albumin Binding Domain™ technology. HNSCC head and neck squamous cell carcinoma. ISS investigator sponsored Phase 1 study.

FINANCIAL AND INVESTMENT GOALS

- Immediate Goals
  - Augment share register with additional sophisticated institutional investors
  - Establish a realistic share price/valuation to facilitate financial options
  - External validation through a funded discovery or development partnership

- Mid- to Longer Term Goals
  - Institutional investment to enable registration studies in lead indication(s)
  - Financing or partnering to advance OV pipeline and explore additional indications

APPENDIX

INTELLECTUAL PROPERTY

Hyaluronidase OV

VCN-01, VCN-11

Composition of Matter (exp 2030)

Methods of Use and Novel Formulations (examination)

Use in Rb (exp 2036)

ODD EU (PDAC)

ODD US (Rb)

Albumin Shield™

VCN-11, Discovery

Composition of Matter (exp 2034)

Methods of Use and Novel Formulations (examination)

Oral β-Lactamase

SYN-004, -006, -007

Composition of Matter (exp 2031-5)

Methods of Use and Novel Formulations (exp 2035-6)

Oral IAP

SYN-020

Manufacturing Know-how (Trade Secret)

Methods of Use and Novel Formulations (applications filed)

Option to additional IP from MGH

Theriva BIOLOGICS

ODD Orphan Drug Designation provides 7 years market exclusivity in US and 10 years in the EU. OV oncolytic virus. PDAC pancreatic ductal adenocarcinoma. Rb retinoblastoma.

EXTENSIVE VCN-01 PHASE 1 CLINICAL EXPERIENCE

>80 Patients Treated in Diverse Cancer Indications

Location	Phase	Indication	Co-therapy	Route	Status	Registry
Multicenter (ESP)	1	Part I: Solid tumor Part II, III: PDAC	Part I: None Parts II,III: Gemcitabine + nab-Paclitaxel	IV	Complete[1]	NCT02045602
Multicenter (ESP)	1	PDAC	Gemcitabine + nab-Paclitaxel	IT	Complete[2]	NCT02045589
Hospital Sant Joan de Déu, Barcelona	1	Retinoblastoma	None	IVit	Ongoing; partial data available	NCT03284268
Institut Català d'Oncologia (ICO)	1	HNSCC	Durvalumab	IV	Treatment complete; Initial data H2'22	NCT03799744
U. Leeds	1	Adult brain tumors	None	IV	Ongoing	ISRCTN 517624869
U. Pennsylvania	1	PDAC, Ovarian	huCART-meso[3]	IV	Ongoing	NCT05057715

Theriva BIOLOGICS

[1]Garcia-Carbonero (2022) J Immunother Cancer 10:e003255. [2]Bazan-Peregrino (2021) J Immunother Cancer 9:e003254. [3]huCART-meso are autologous T cells engineered to express an extracellular single chain variable fragment (scFv) with mesothelin specificity. HNSCC head and neck squamous cell carcinoma. IV intravenous. IT intratumoral. IVit intravitreal.

MOST COMMON IV VCN-01 RELATED AEs [NCT02045602]

ADVERSE EVENTS[1]	Part I (Alone, n=16)		Part II (Concomitant, 12)[2]		Part III (Sequential, 14)[3]	
	Grade 1-2	Grade ≥3	Grade 1-2	Grade ≥3*	Grade 1-2	Grade ≥3
Febrile neutropenia	-	-	-	2 (16.7%)	-	-
Neutropenia/Neutrophil count decreased	2 (12.5%)	-	1 (8.3%)	1 (8.3%)	-	-
Thrombocytopenia/Platelet count decreased	1 (6.3%)	1 (6.3%)	3 (25.0%)	4 (33.3%)	2 (14.3%)	-
Diarrhea	3 (18.8%)	-	1 (8.3%)	-	-	1 (7.1%)
Nausea	2 (12.5%)	-	3 (25.0%)	-	3 (21.4%)	-
Vomiting	3 (18.8%)	-	2 (16.7%)	-	3 (21.4%)	-
Asthenia/Fatigue	2 (12.5%)	-	5 (41.7%)	1 (8.3%)	3 (21.4%)	-
Pyrexia/Influenza-like Illness	12 (75.0%)	1 (6.3%)	8 (66.7%)	-	12 (85.7%)	-
Transaminase increases (ALT, AST)	2 (12.5%)	3 (18.8%)	1 (8.3%)	1 (8.3%)	2 (14.3%)	2 (14.3%)
Pancreatic enzyme increase (lipase, amylase)	1 (6.3%)	3 (18.8%)	-	-	-	-
Decreased appetite	3 (18.8%)	-	3 (25.0%)	-	-	-
Arthralgia	2 (12.5%)	-	-	-	-	-
Musculoskeletal pain	3 (18.8%)	-	4 (33.3%)	-	-	-
Dizziness	1 (6.3%)	-	1 (8.3%)	-	-	-
Headache	1 (6.3%)	-	1 (8.3%)	-	1 (7.1%)	-
Dyspnea	2 (12.5%)	-	-	-	-	-
Hypotension	2 (12.5%)	-	1 (8.3%)	-	-	-

*Part II: one patient at the highest dose ($1x10^{13}$ vp) died from a combination of thrombocytopenia (Grade 4) and enterocolitis (Grade 5)

Theriva BIOLOGICS

[1]Garcia-Carbonero (2022) J Immunother Cancer 10:e003255. [2]Concomitant IV VCN-01 $3.3x10^{12}$ or $1.0x10^{13}$ vp/patient administered same day as first dose of SoC IV gemcitabine/nab-paclitaxel. [3]Sequential IV VCN-01 $3.3x10^{12}$ or $1.0x10^{13}$ vp/patient administered 7-days prior to first dose of SoC.

VIRAGE PHASE 2 CLINICAL TRIAL – DIFFERENTIATORS

- ✓ First-line treatment of metastatic PDAC patients
- ✓ Direct comparison with standard-of-care chemotherapy in the same trial
- ✓ Open label provides real-time opportunity to review emerging VCN-01 treatment effects
- ✓ Interim analysis based on secondary endpoints may enable early engagement with regulatory agencies regarding requirements for approval
- ✓ Repeated dosing of VCN-01 may improve treatment outcomes
- ✓ Orphan Drug Designation to facilitate regulatory interactions and provide market exclusivity

Theriva BIOLOGICS

[1]Orphan Drug Designation has been obtained in the USA and Europe

TOXICITY COMBINATION VCN-01 & Durvalumab

Most Common IV VCN-01 Related AEs (IV in HNSCC + Durvalumab)

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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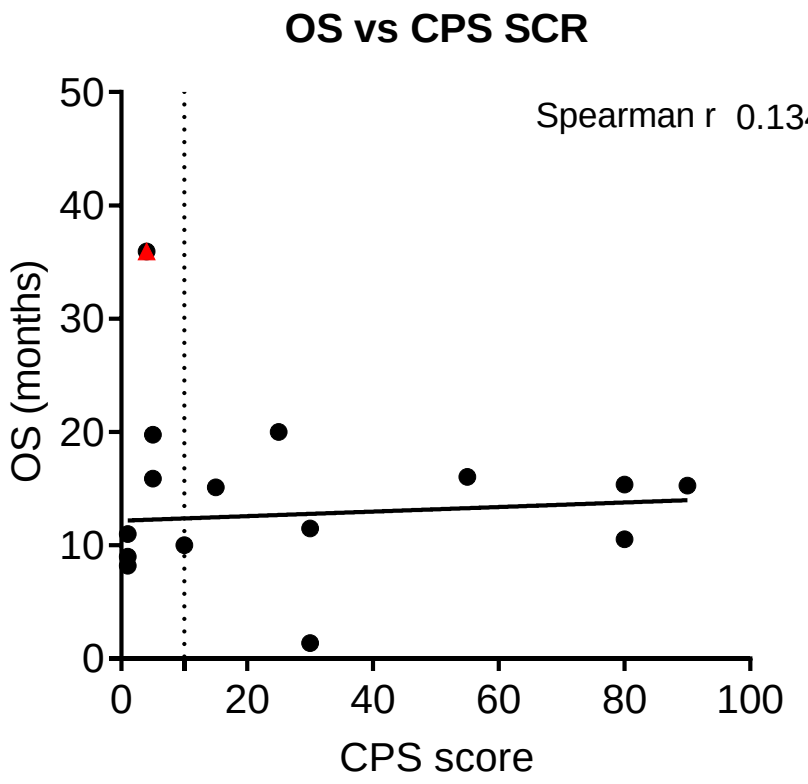
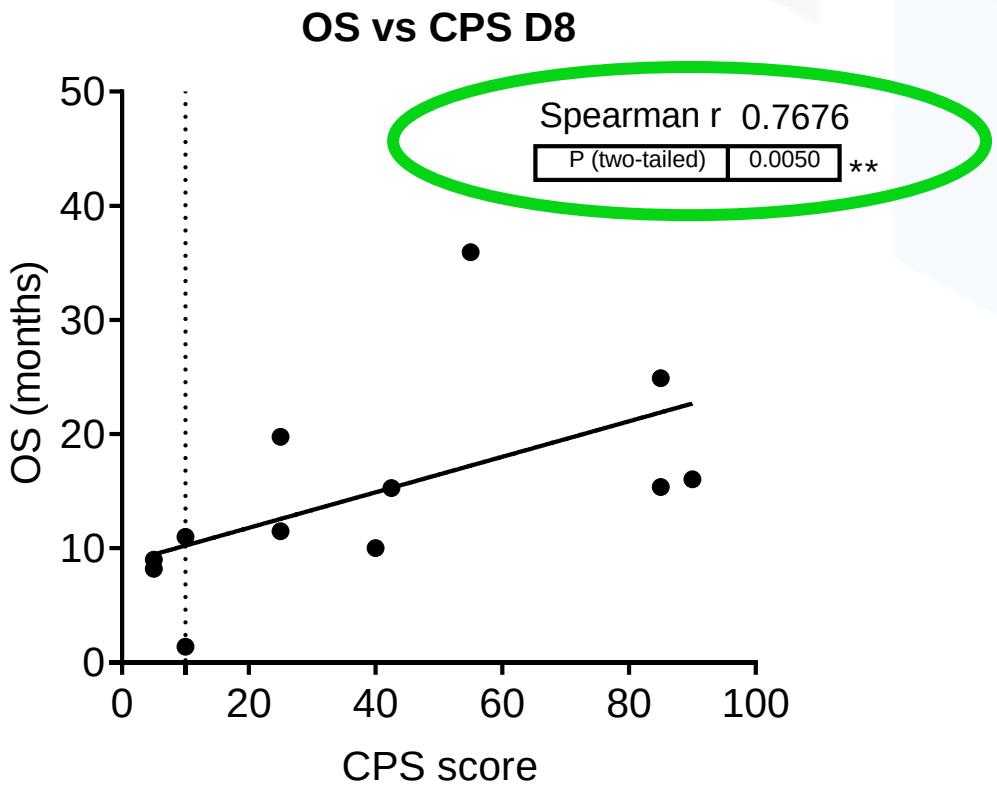
EXTENDED SURVIVAL with VCN-01+DURVALUMAB

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

Pre-treatment



Day 8 after VCN-01 dose



Initial evidences suggests that VCN-01 induced PD-L1 upregulation could enhance patient survival

Theriva BIOLOGICS

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

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 LA 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. Pancreatology 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

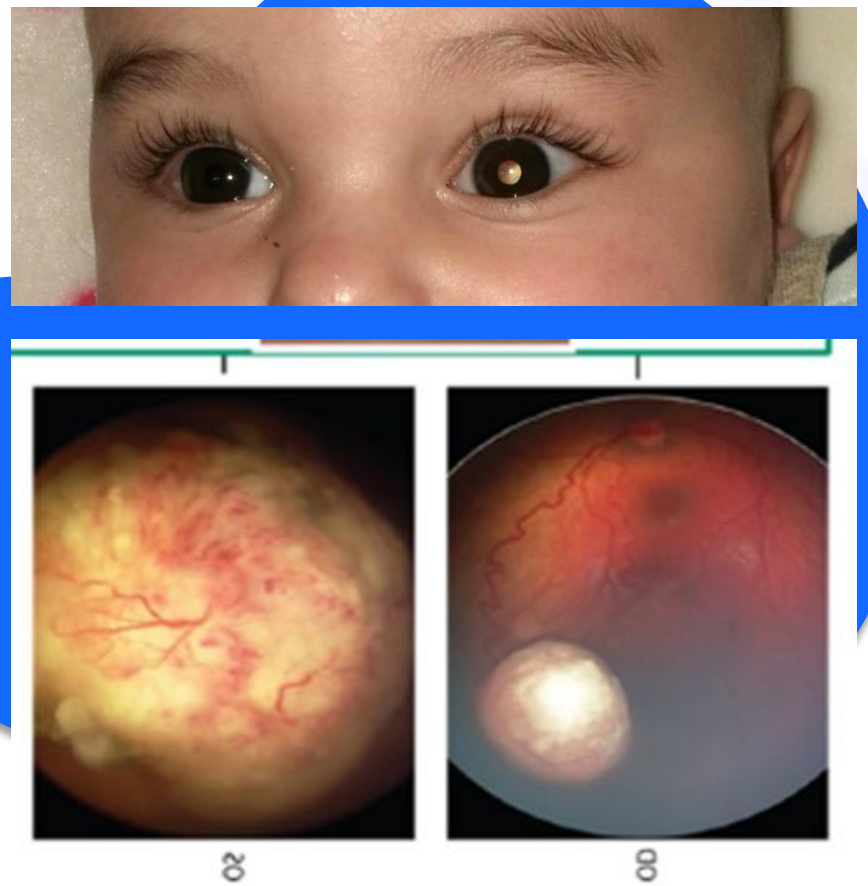
Ancona-Lezama D et al. (2020) Modern treatment of retinoblastoma: a 2020 review. Indian J Ophthalmol 68:2356-65

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

VCN-01 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



Theriva BIOLOGICS

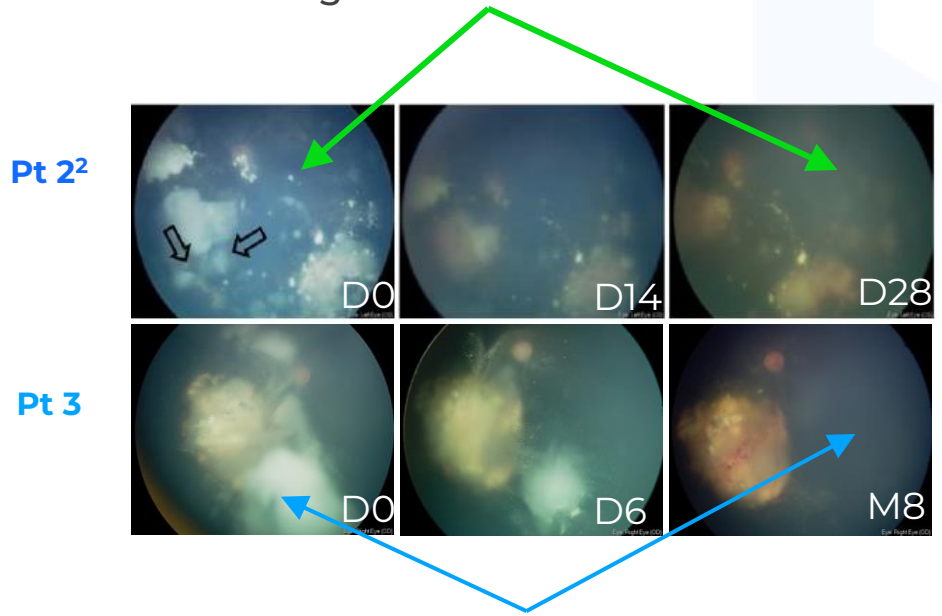
[1]https://www.cancer.org/cancer/retinoblastoma/about/key-statistics.html. [2]Stacey (2021) Ophthalmology 128:1369. [3]One Retinoblastoma World Map https://map.1rbw.org/. [4]For additional details and references see Appendix. IMAGE: Courtesy of Hospital Sant Joan de Déu, Barcelona

VCN-01 in Retinoblastoma

- On-going single center, open-label, dose escalation study of intravitreal (IVit) VCN-01[1-3]
  - Children aged 1-12 years (n=6 to date)
  - 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=4) on days 1 and 15
- Promising antitumor activity and appropriate safety and tolerability at RP2D
  - Enucleation avoided in 1 of 6 patients to date
  - Low VCN-01 dose and/or damage from prior chemotherapy meant eye could not be saved in 5 patients
- Earlier VCN-01 intervention anticipated to have better outcomes

Promising Results in 2 of the Patients Treated to date with High Dose VCN-01

Reduced number and size of tumor vitreous seeds following VCN-01 administration[2]



Complete tumor regression[3]

Theriva BIOLOGICS

[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.

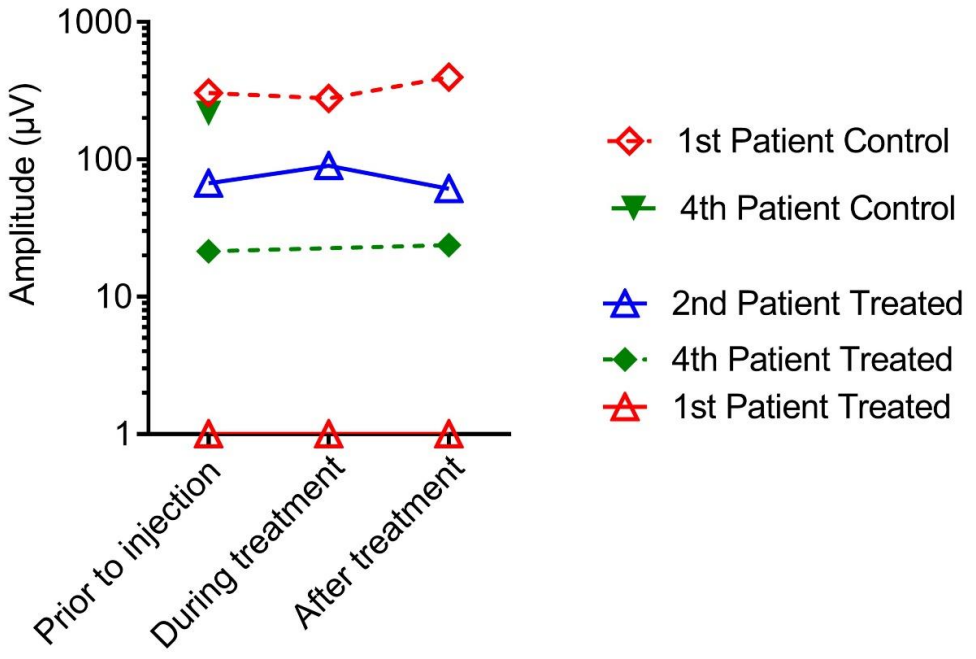
Interim Safety Data for Intravitreal VCN-01

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	4	2	50%	2	50%
Periphlebitis	4	1	25%	0	0%

- VCN-01 was reasonably well tolerated after intravitreal administration[2], although some turbidity and vitritis associated with intravitreal inflammation was observed
- Intravitreal inflammation was managed with local and systemic administration of anti-inflammatory drugs
- VCN-01 did not appear to change retinal function (electroretinographic signaling)
- VCN-01 does not replicate in healthy retinal tissue[3]

Stable Electroretinographic Signals



[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.

Retinoblastoma Project Clinical Development

- Developing a clinical protocol for an open-label, multinational study
  - Rb patients with vitreous seeds
  - IVit VCN-01 in combination with chemotherapy (no defined SoC)
  - PI Dr. Guillermo Chantada, MD PhD[1]
- Status
  - Clinical study design being discussed with KOLs
  - Analyzing regulatory landscape and recruitment rates in different geographical regions
  - US Orphan Drug Designation
  - Pre-IND meeting with FDA in Q4 2023

Theriva BIOLOGICS

[1]Principal Researcher, Associate Physician, Hospital Sant Joan de Déu, Barcelona, Spain; Scientific Director, Pediatric Hemato-Oncology Service of the Hospital Universitario Austral, Argentina