



Corporate Overview

October 2022

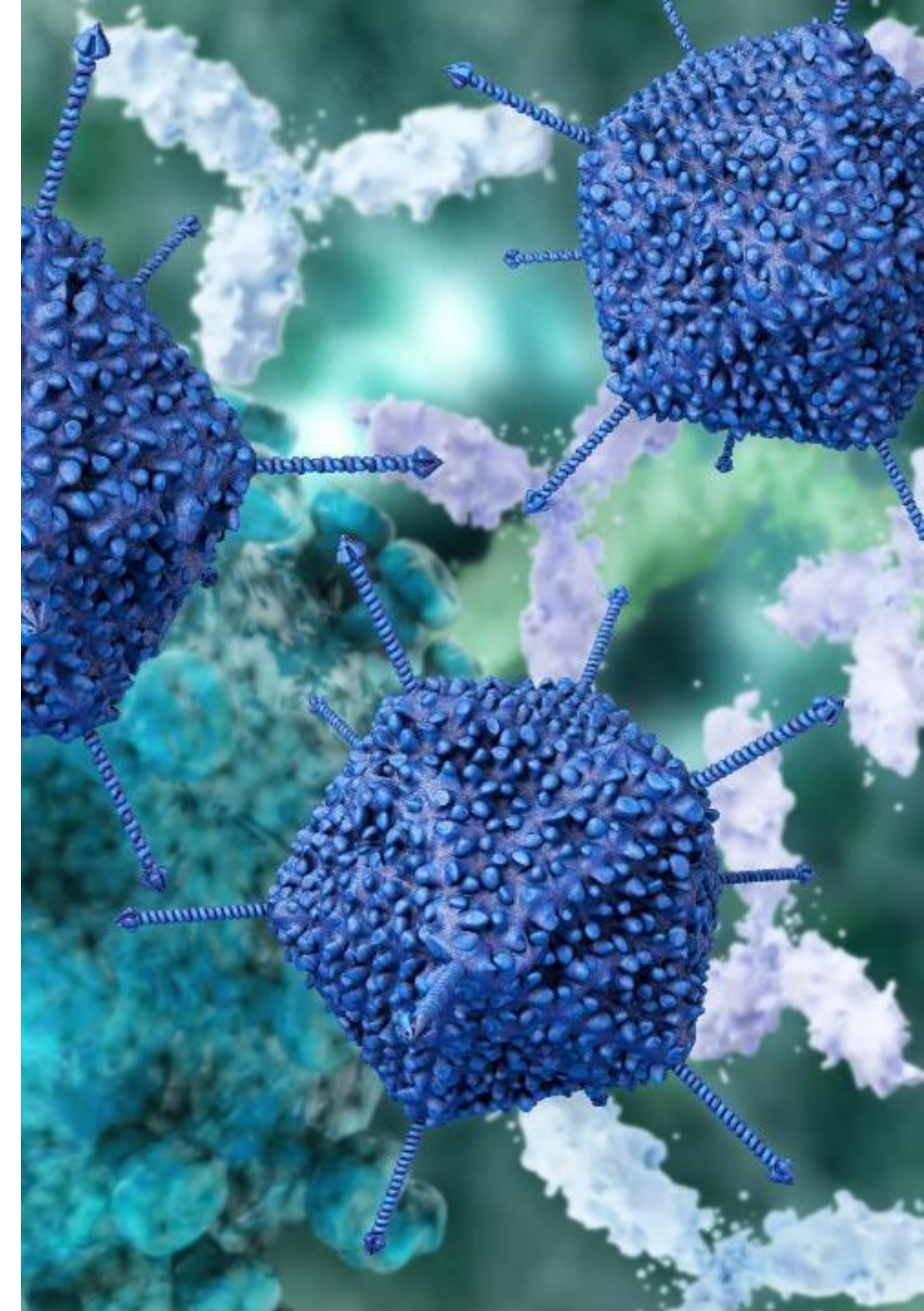
Forward Looking Statements










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 the potential of VCN-01 and its ability to overcome key oncolytic virus challenges, oncolytic viruses being promising cancer therapeutics, near term clinical advancement of VCN-01 including initiation of a Phase 2 PDAC clinical trial in Q4 2022 and an Rb Company sponsored clinical trial late 2023, the proposed PDAC Phase 2 clinical trial design and the potential of the albumin shield to enhance the OV systemic delivery and the potential of the other Theriva Biologics' product candidates. 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 a Phase 2 PDAC clinical trial in Q4 2022 and an Rb Company sponsored clinical trial late 2023; the ability to 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 VCN's and 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, 2021 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 (NYSE American: [TOVX](#)) is developing unique oncolytic viruses (OVs) optimized for systemic administration and selective tumor destruction
- Lead clinical product [VCN-01](#) is poised to enter advanced clinical studies in metastatic pancreatic ductal adenocarcinoma and retinoblastoma
- Proprietary [Albumin Shield™](#) platform enables development of next-generation products for additional hard-to-treat cancers
- Additional clinical programs provide opportunities for value generation in a range of indications
- Programs supported by strong current cash position with runway to 2024¹

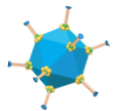


Pipeline

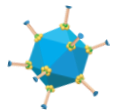
Technology	Candidate	Target	Pre-IND	Phase 1	Phase 2	Collaborators	Status*
Stroma Degrading Oncolytic Virus (OV)	VCN-01	Pancreatic Cancer (IV) with gemcitabine/nab-paclitaxel	<div><div></div></div>				Ph 2 Trial Initiation Expected Q4'22 (ODD EU)
		Retinoblastoma (IVit)	<div><div></div></div>				Trial Initiation Expected H2'23 (ODD US)
		HNSCC (IV) + durvalumab	<div><div></div></div>				Enrollment Complete Initial Data H2'22
		Solid Tumors – Brain, Ovarian, PDAC (IV)	<div><div></div></div>			 	Investigator Sponsored Studies U. Penn initiated, U. Leeds screening
Oral β -lactamase	SYN-004	Prevention of aGVHD in allo-HCT	<div><div></div></div>				Cohort 1 Phase 1b/2a Topline Data H2'22
Oral IAP	SYN-020	Potential indications include NAFLD/NASH, celiac, radiation enteritis	<div><div></div></div>			 MASSACHUSETTS GENERAL HOSPITAL	Reported MAD Topline Data Q2'22
Albumin Shield OVs	VCN-11	Solid tumors (IV)	<div><div></div></div>			 	Ongoing Preclinical Studies

Oncolytic Viruses are Promising Cancer Therapies

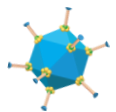
Opportunities



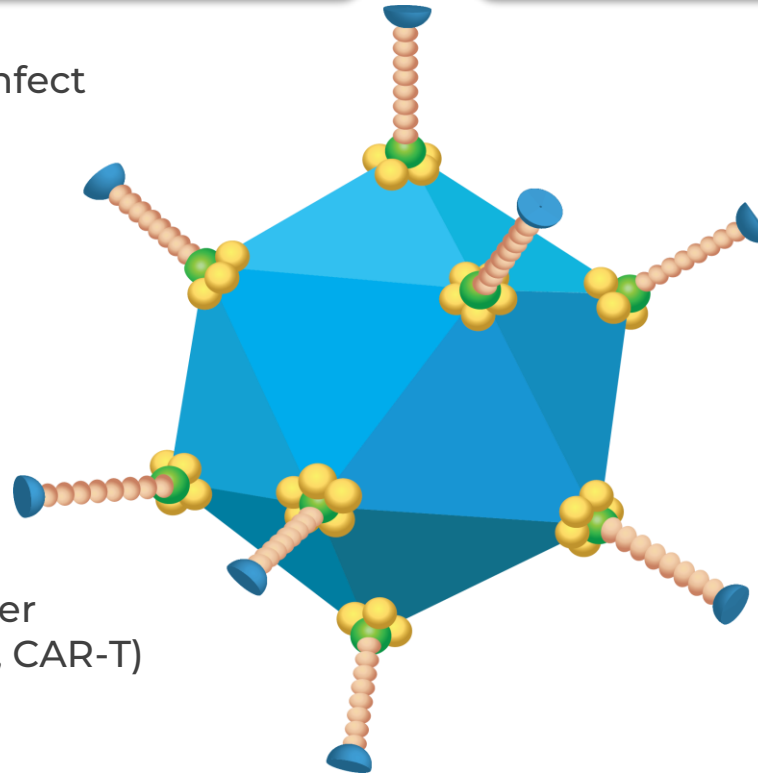
Can be engineered to selectively infect and directly destroy tumor cells



Can induce persistent anti-tumor immune responses



Can be combined with other cancer therapies (e.g. chemotherapy, CPI, CAR-T)



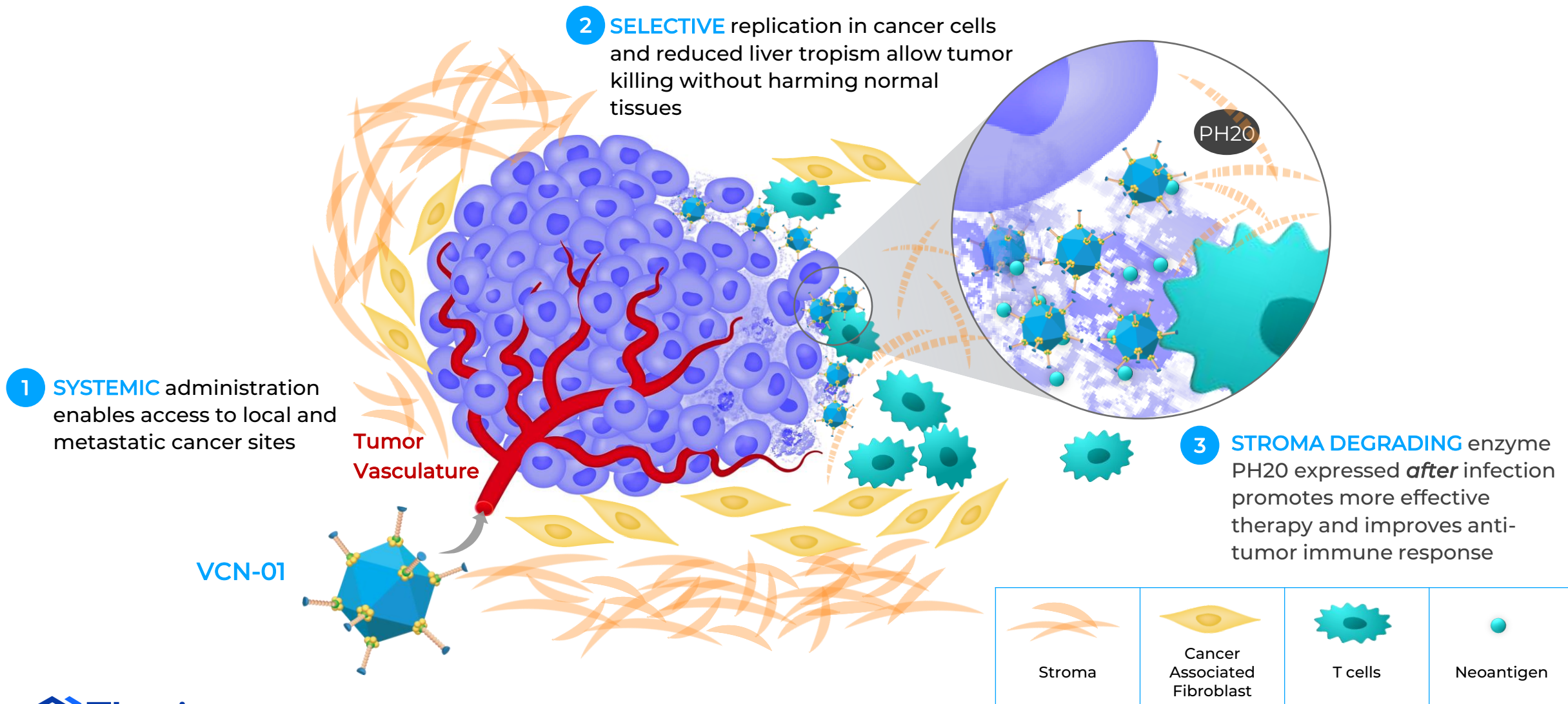
Challenges

Administration: OV's have typically required localized injection to deliver sufficient virus, avoid off-target effects

Access: physical and immuno-suppressive stroma barrier inhibits tumor penetration by cancer therapies

Availability: low tolerated doses, patient antiviral response, and liver clearance can all limit virus delivery to the primary tumor and metastases

Unique Mechanism of Action for Theriva OV Products



Extensive VCN-01 Phase 1 Clinical Experience

Collaborating with world-leading institutions, 76 patients treated to date

Location	Phase	Indication	Co-therapy	Route	Status	NCT or Other
Multicenter (ESP)	1	Part I: Solid tumor Part II: PDAC Part 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	Partial data available	NCT03284268
Institut Català d'Oncologia (ICO)	1	HNSCC	Durvalumab	IV	Enrollment complete; initial data H2'22	NCT03799744
U. Leeds	1	Adult brain tumors	None	IV	Screening	ISRCTN 517624869
U. Pennsylvania	1	PDAC, Ovarian	huCART-meso ³	IV	Ongoing	NCT05057715

VCN-01 Clinical Program in PDAC



Pancreatic Ductal Adenocarcinoma

- Pancreatic adenocarcinoma (PDAC) is a deadly cancer with the highest mortality of all solid tumors
 - Accounts for the 3rd highest no. cancer deaths in the US each year (4th in EU)^{1,2}
 - Median survival 4-6 months from diagnosis; 1 year survival 24%
- Treatment options for metastatic PDAC are limited³
 - First-line therapies include gemcitabine + nab-paclitaxel and (m)FOLFIRINOX,
 - Checkpoint inhibitors have been largely ineffective
- PDAC has a dense stroma that acts as a physical and immunosuppressive barrier to therapy
 - Stromal hyaluronan is associated with low immune response and poor prognosis⁴



Pancreatic adenocarcinoma resected from the pancreas body and tail

Positive VCN-01 Phase 1 Data Encourage PDAC Phase 2 Trial

Phase 1, multicenter, open-label, dose escalation study of single IV doses of VCN-01 alone or with standard-of-care gemcitabine/nab-paclitaxel (SoC)¹

ARM I *Monotherapy* VCN-01 dose finding, primarily colorectal cancer

ARM II *Concomitant* VCN-01 administered same day as first dose of SoC in PDAC patients

ARM III *Sequential* VCN-01 administered 7-days before first dose of SoC in PDAC patients

Sequential dosing regimen is being advanced to a Phase 2 clinical trial

Favorable Survival with VCN-01 + SoC Compared to Published SoC alone

VCN-01 Sequential Regimen ¹	VCN-01 + SoC	Published SoC alone ²
Overall Survival (n)	median months	
3.3x10 ¹² vp/patient (6)	13.1	
1.0x10 ¹³ vp/patient (6)	20.8	
Combined (both doses) (12)	13.5	8.5
Overall Response Rate (n)	n (%)	
3.3x10 ¹² vp/patient (6)	1 (16.7%)	
1.0x10 ¹³ vp/patient (6)	5 (83.3%)	
Combined (both doses) (12)	6 (50%)	23%
Length of Survival	n (%)	
Survival > 12 months	8 (75%)	
Survival > 27 months	3 (25%)	

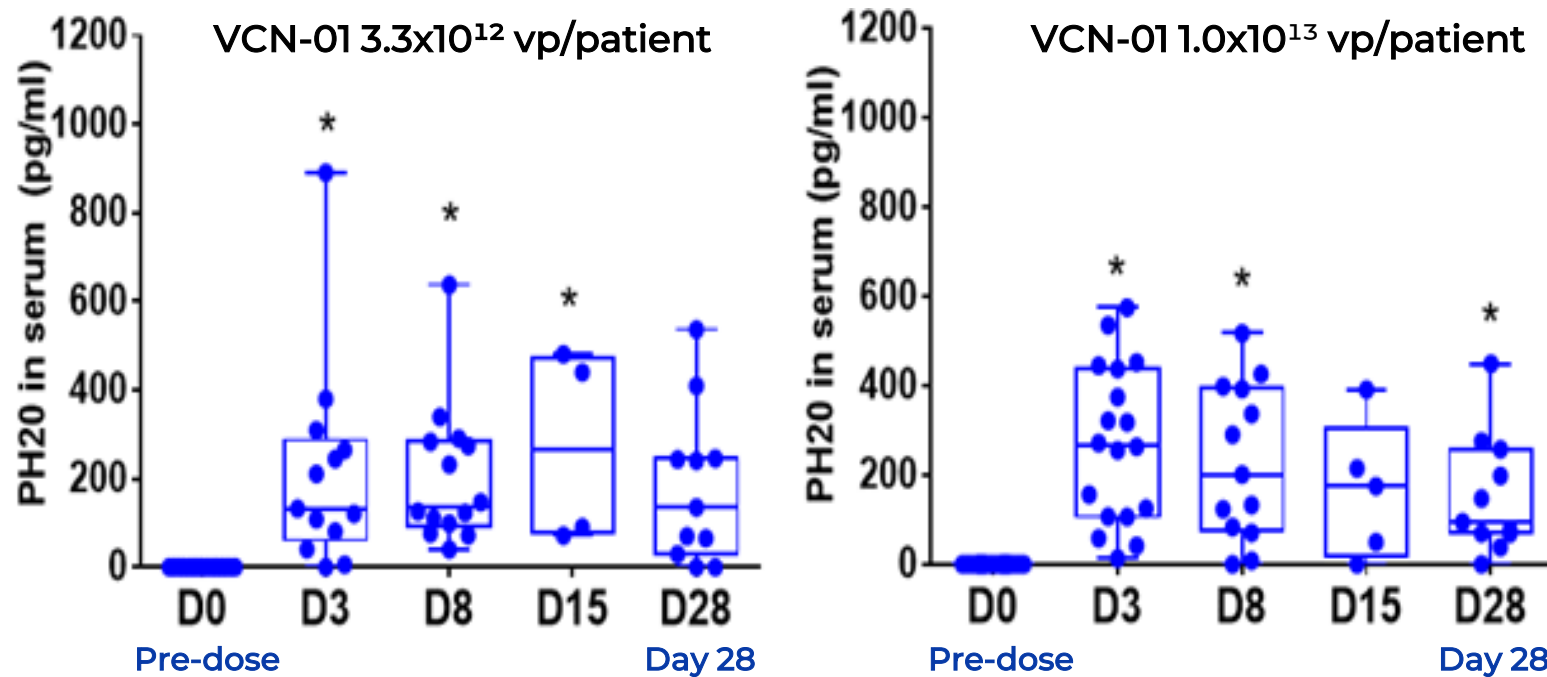
Most Common IV VCN-01 Related AEs (Multicenter, Spain)¹

Adverse Events	Part I (Alone, n=16)		Part II (Concomitant, 12) ²		Part III (Sequential, 14) ³	
CTCAE Grade	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 (1x10¹³ vp) died from a combination of thrombocytopenia (Grade 4) and enterocolitis (Grade 5)

Oncolytic Viruses are Promising Cancer Therapeutics

Sustained PH20 levels in serum of PDAC patients treated with IV VCN-01

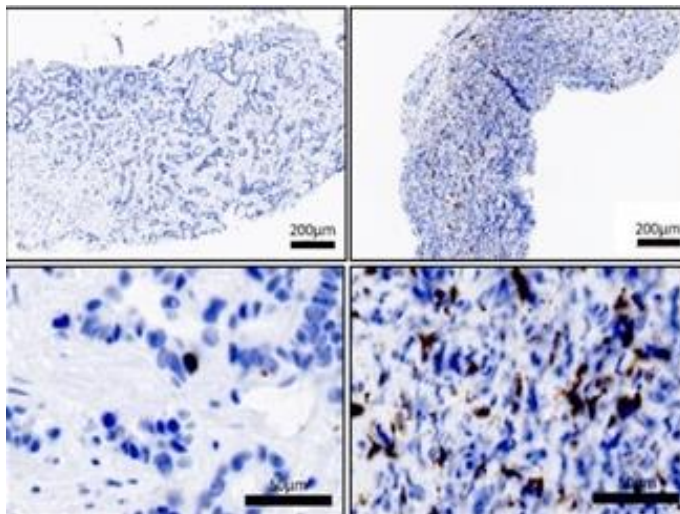


Built-in biomarker: hyaluronidase (PH20) levels in patient sera are linked to viral replication and demonstrate sustained VCN-01 activity in tumors

VCN-01 Elicits an Anti-Tumor Inflammatory Response

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

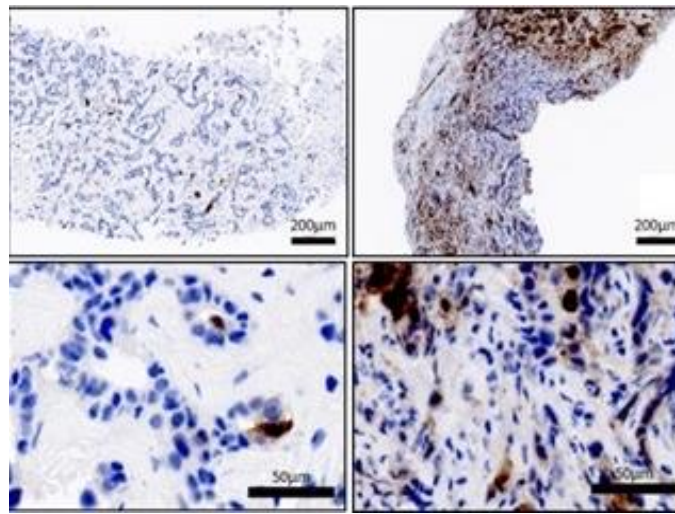
CD8⁺ lymphocyte infiltration



Pre-Dose

Day 8

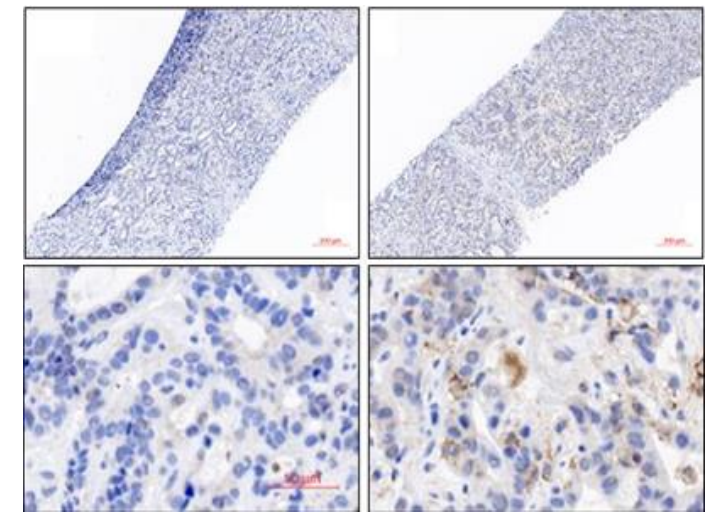
IDO upregulation



Pre-Dose

Day 8

PD-L1 upregulation



Pre-Dose

Day 8

Immunohistochemistry staining of biopsies from **hepatic metastases** of a PDAC patient treated with IV VCN-01

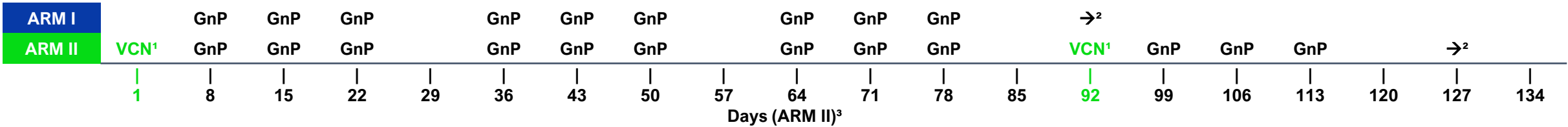
Proposed VCN-01 Phase 2 Clinical Trial in PDAC

- Enrollment

- Open-label, randomized Phase 2b study conducted at up to 25 sites across the US, Spain and Germany
- Patients ≥18 y.o. with histologically confirmed, first line metastatic pancreatic ductal adenocarcinoma
- Established clinical standard-of-care (SOC) therapy is gemcitabine/nab-paclitaxel (Abraxane®)
- Adequate baseline organ function per defined hematologic, liver, renal and nutritional criteria

- Treatment Arms (Randomization 1:1, N=92)

- Arm I: Gemcitabine/nab-paclitaxel standard of care (GnP 28-day cycles)
- Arm II: GnP with VCN-01 (IV; days 1 and 92) administered 7-days before first dose of GnP in the cycle



Proposed VCN-01 Phase 2 Clinical Trial in PDAC

- **Primary Endpoints**

- Time from randomization until death in both arms (OS).
- To evaluate the safety & tolerability of VCN-01, i.v administered at Week 1 & Week 14 in Arm II.

- **Secondary Endpoints**

- Time to progression (TTP) or progression free survival (PFS)
- Objective Response rate (ORR).
- Disease control rate (DCR)
- Landmark 1-year survival and PFS at the 1-year landmark
- Duration of response (DoR)

- **Exploratory Endpoints**

- Circulating immune markers in serum, VCN-01 genomes in blood, PH20 levels in serum, neutrophil/lymphocyte ratio, and serum levels of neutralizing anti-VCN-01 antibodies (Anti-Ad-NABs)
- Radiomic analysis of computerized tomography (CT) images
- Quality of Life (QoL)

Proposed VCN-01 Phase 2 Clinical in PDAC

- Sample Size Considerations

- Median OS in control ARM I ~10.6 months; OS ≥ 15 months in treatment ARM II considered clinically meaningful by PI
- 57 total events needed to provide 80% power for OS endpoint (1-sided)
- Interim analysis (IA) of OS, landmark OS12, and/or tumor response may enable early discussion with regulatory agencies
- Timing of potential IA to be determined based on real-time monitoring of treatment effect

- Status

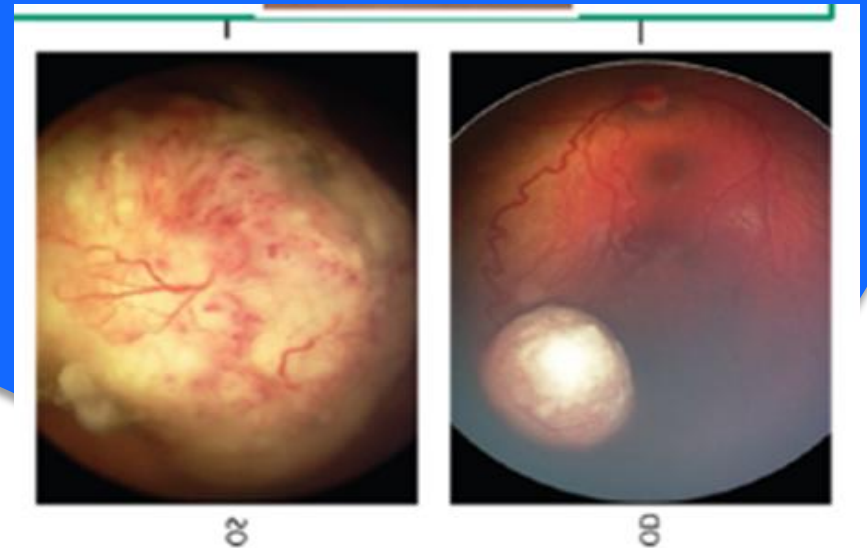
- Protocol completing regulatory and IRB/EC review in US, Spain and Germany
- Orphan Drug Designation in EU (application to be submitted in USA)
- PI Dr. Manuel Hidalgo Medina, MD PhD¹
- Anticipate trial initiation [Q4 2022](#)

VCN-01 Clinical Program in Retinoblastoma



Retinoblastoma, a Rare Pediatric Malignancy

- Retinoblastoma (Rb) is an orphan indication that accounts for ~2-3% of all childhood cancers¹
- 200-300 cases each year in the USA, EU²⁻⁴
- 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

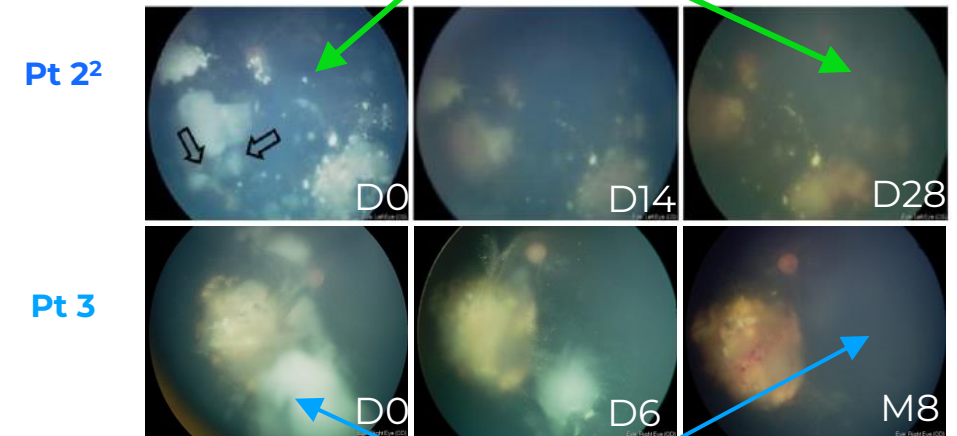


VCN-01 in Retinoblastoma

- On-going single center, open-label, dose escalation study of intravitreal (IVit) VCN-01¹⁻³
 - 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 2.0×10^9 vp per eye (n=1) or 2.0×10^{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 4 patients to date
 - Low VCN-01 dose and/or damage from prior chemotherapy meant eye could not be saved in 3 patients
- Earlier VCN-01 intervention anticipated to have better outcomes

Promising Results in 2 of the 3 Patients Treated to Date with High Dose VCN-01

Reduced number and size of tumor vitreous seeds following VCN-01 administration²



Complete tumor regression³

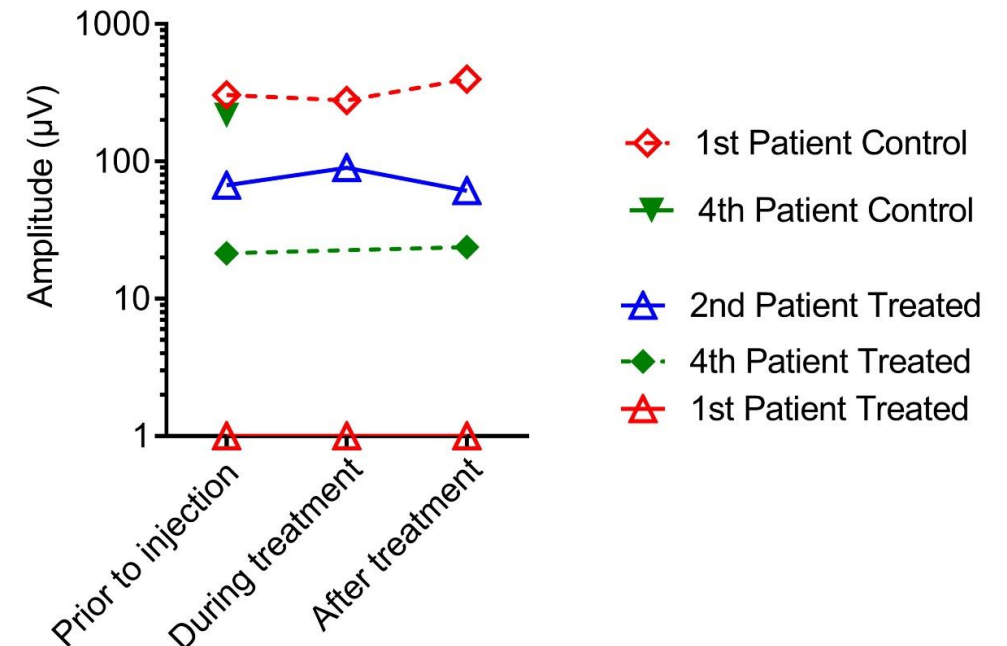
Interim Safety Data for Intravitreal VCN-01

Two Intravitreal VCN-01 Doses of 2.0×10^9 or 2.0×10^{10} vp per eye¹

Adverse Reaction	Pts	All Grades		Grade ≥ 3	
CTCAE grade	N	n	%	n	%
Uveitis	4	2	50%	2	50%
Periphelebitis	4	1	25%	0	0%

- VCN-01 was reasonably well tolerated after intravitreal administration², 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 tissue³

Stable Electroretinographic Signals



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 IVit chemotherapy (no defined SoC)
 - PI Dr. Guillermo Chantada, MD PhD¹
- Status
 - Clinical study design being discussed with KOLs
 - Analyzing regulatory landscape and recruitment rates in different geographical regions
 - US Orphan Drug Designation
 - Anticipate trial initiation [late 2023](#) (contingent on regulatory agreement)

VCN-01 Clinical Summary

Extensive Phase 1 Clinical Experience

- Administered to 76 cancer patients to date (61 by IV dosing)
- Alone or in combination with chemotherapy, immunotherapy

Clinical Demonstration of MOA

- High levels of viral replication and PH20 expression in tumors
- Increased tumor immunogenicity and tumor inflammation

Strong Support for Phase 2 Trials

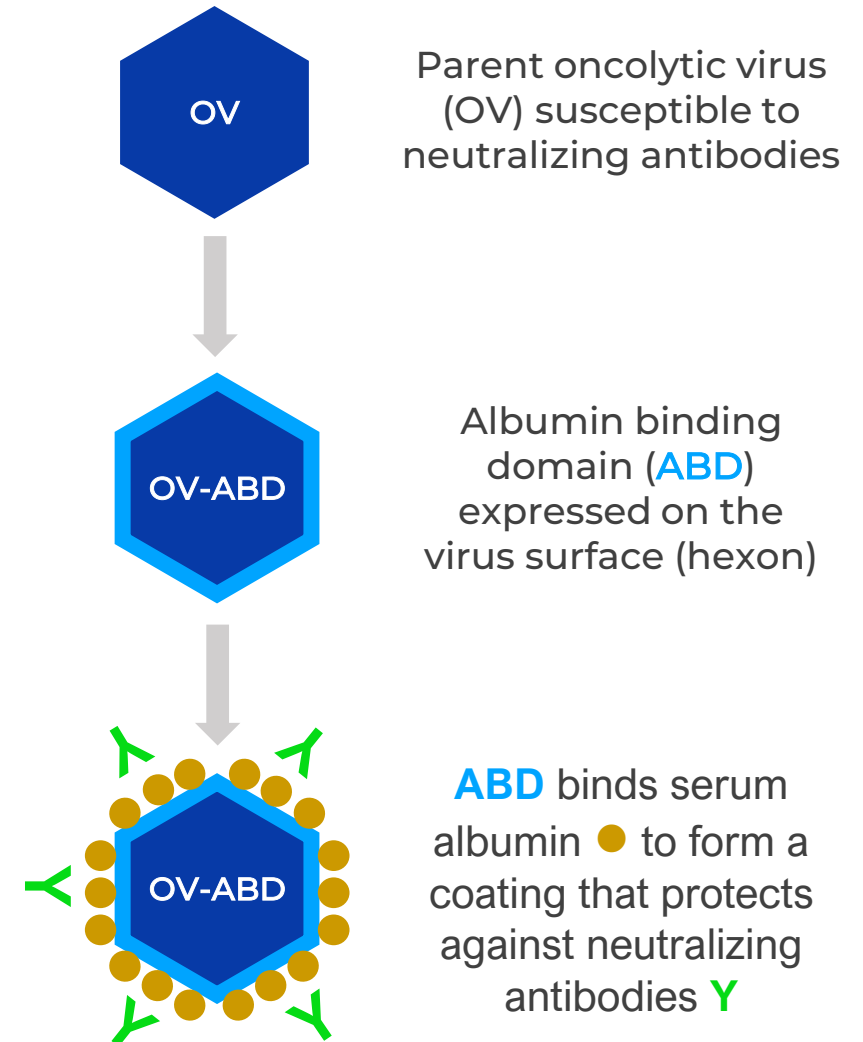
- Tumor responses in PDAC and Rb patients treated with VCN-01
- Appropriate VCN-01 safety and tolerability for patient population
- Favorable survival in PDAC patients treated with VCN-01 plus SoC chemotherapy compared to published data for SoC alone



Opportunities for Long Term Growth

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



VCN-01 Near Term Clinical Advancement

Common Features

Clinically-tested Adenovirus Expressing
PH20 Hyaluronidase TO DEGRADE Stroma

+

Albumin Shield™
To Prevent Neutralization By Circulating
Anti-viral Antibodies To Facilitate IV
Multidosing

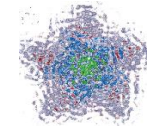
+

Unique Multifunctional Proteins
To Turn Cold Tumors Hot

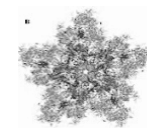
Product Specific Features



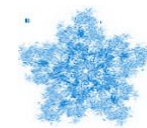
VCN-11: Hyaluronidase alone



Hyaluronidase + Toxins



Hyaluronidase + Immunomodulators



Hyaluronidase + Other

Albumin Shield platform invites potential licensing opportunities



VCN-01 Clinical Program Phase 1 Trial in Head & Neck Squamous Cell Carcinoma

NCT03799744 : Systemic VCN-01 in HNSCC & Durvalumab (α -PD-L1)

Design

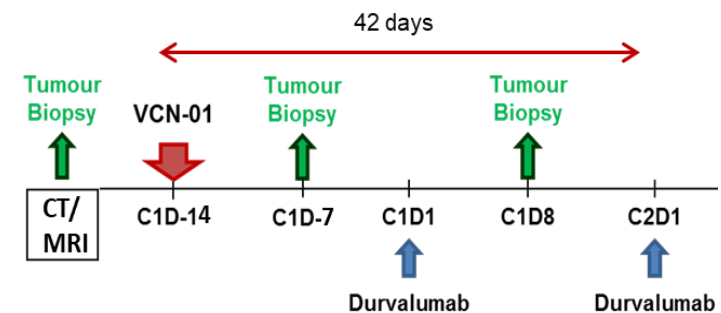
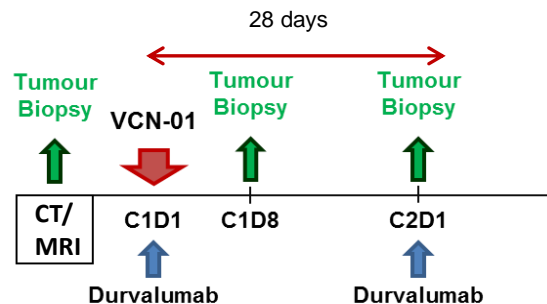
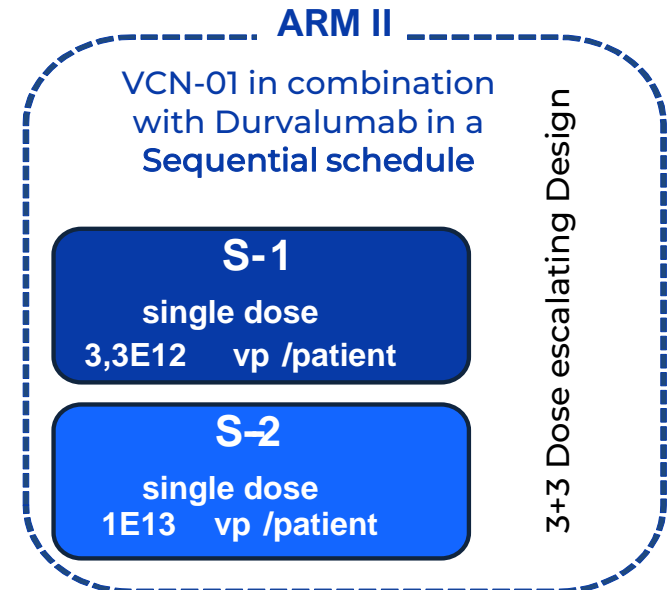
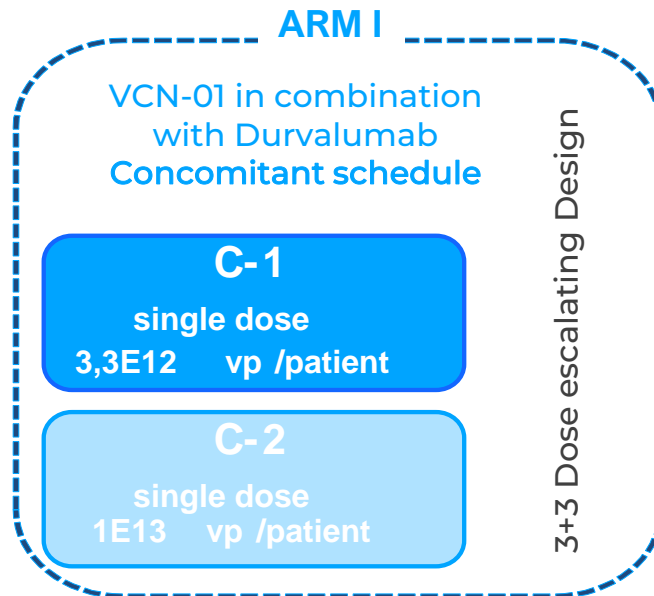
Study Population:

Patients with metastatic squamous cell carcinoma of the head & neck previously treated with anti-PD(L)1 agents (R/MHNSCC)

Sites:



Pre-screening for anti-hAd5 neutralizing antibodies
(65-70% recruiting rate at selected threshold)



NCT03799744: Systemic VCN-01 in HNSCC & Durvalumab (α -PD-L1)

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

Adverse Reactions CTCAE Grade	Arm I (Concomitant, 6) ²		Arm II (Sequential, 14) ³	
	Grade 1-2	Grade ≥ 3	Grade 1-2	Grade ≥ 3
Pyrexia	2 (33,0%)	-	8 (57,1%)	-
Influenza like illness	3 (50,0%)	-	5 (35,7%)	2 (14,2%)
Asthenia/Fatigue	2 (33,0%)	-	6 (42,8%)	1 (7,1%)
AST increased	4 (66,7%)	1 (16,6%)	3 (21,4%)	-
ALT increased	3 (50,0%)	1 (16,6%)	2 (14,2%)	-
Decreased Appetite	1 (16,6%)	-	4 (35,7%)	-
Lymphocyte count decreased	1 (16,6%)	-	-	3 (21,4%)
Myalgia	-	-	4 (35,7%)	-
Hypotension	-	-	3 (21,4%)	-
Chills	1 (16,6%)	-	2 (14,2%)	-
Vomiting	1 (16,6%)	-	2 (14,2%)	-
Anemia	2 (33,0%)	-	1 (7,1%)	-
Nausea	-	-	2 (14,2%)	-
Headache	-	-	2 (14,2%)	-
Erythema	1 (16,6%)	-	1 (7,1%)	-
Hepatic Function Abnormal	-	1 (16,6%)	-	-
Guillain-Barre Syndrome	-	-	-	1 (7,1%)
Hepatic enzymes increased	-	-	-	1 (7,1%)
GGT Increased	-	-	-	1 (7,1%)

NCT03799744 : Analysis of MoA in Clinical Samples

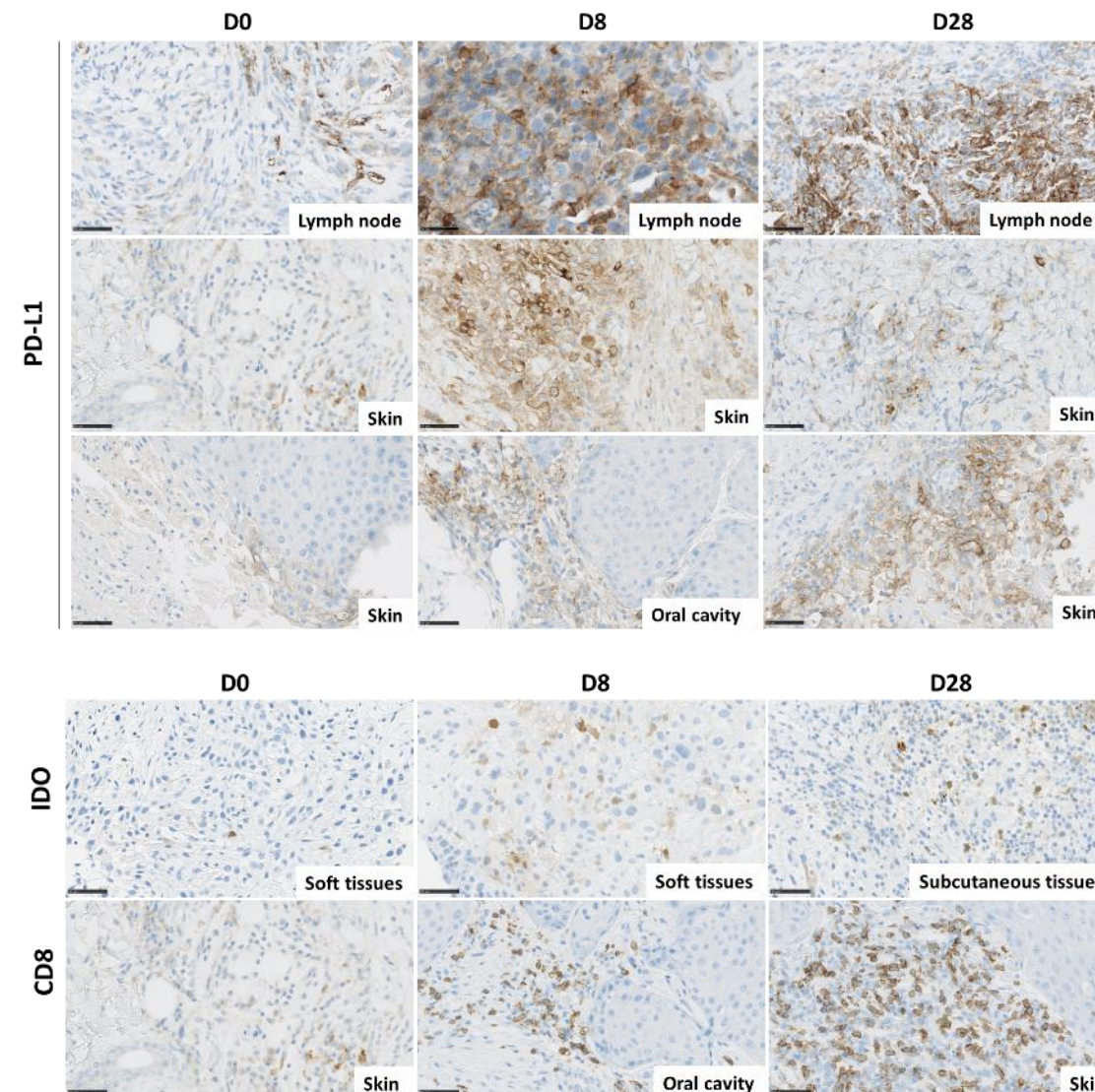
VCN-01 induces up-regulation of PD-L1 in tumor cells

	CD8 /Treg axis	PD-1 / PD-L1 axis	IFNg/ IDO pathway	CTLA4 pathway
D8	55% ↓Tregs* (6/11)	55% ↑PD-1 (6/11)	64% ↑IDO (7/11)	36% ↑CTLA-4 (4/11)
	64% ↑CD8 (7/11)	73% ↑PD-L1 (8/11)		
D28	63% ↓Tregs* (5/8)	56% ↑PD-1 (5/9)	60% ↑IDO (6/10)	33% ↑CTLA-4 (3/9)
	50% ↑CD8 (5/10)	80% ↑PD-L1 (8/10)		

Summary of immune markers variations by IHC of all paired biopsies (Sequential & Concomitant Arm samples). % of samples showing modulation (positive / total analyzed samples)

*Including FoxP3 & CD25 staining

VCN-01 could favor pembrolizumab prescription in 1st line metastatic SSCHN for patients with CPS <1

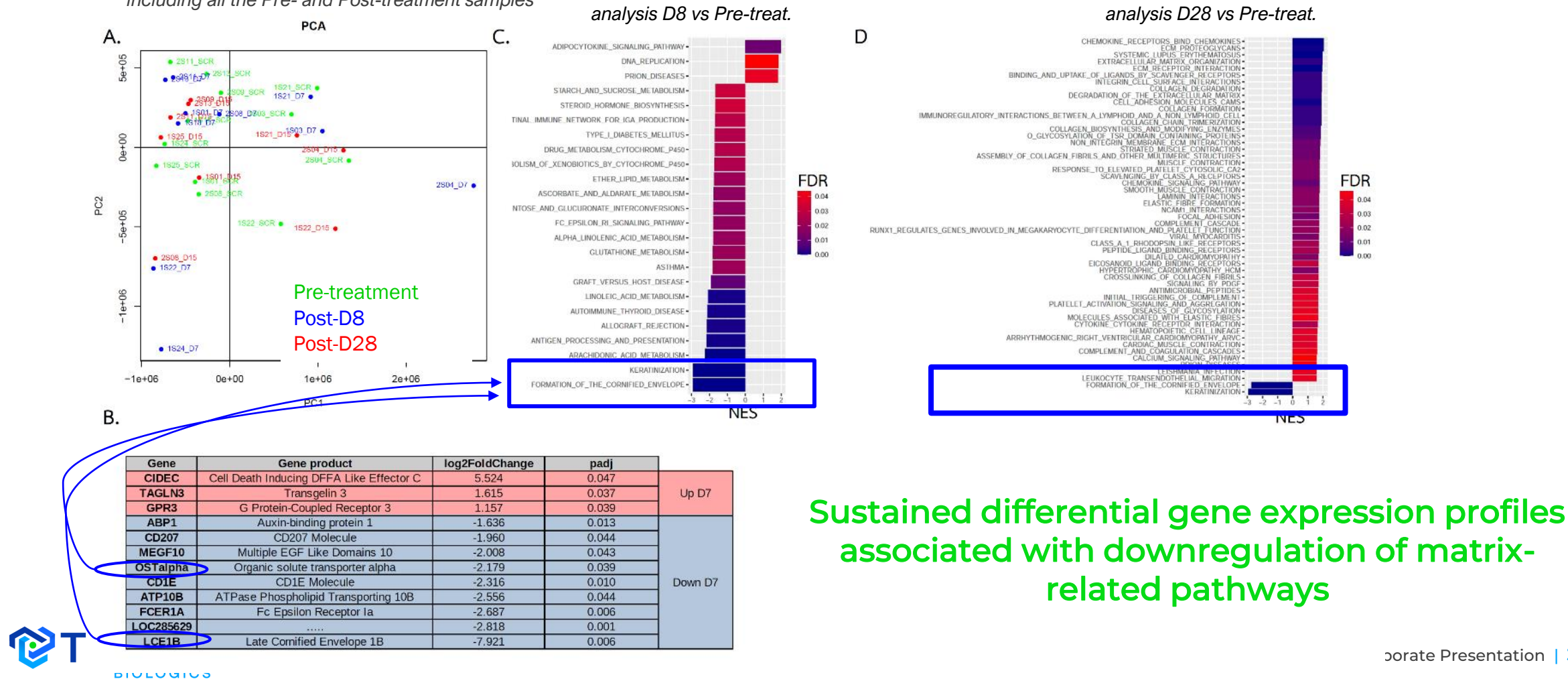


Trial NCT03799744 : Analysis of MoA in Clinical Samples

VCN-01 induces Transcriptomic Changes in Tumor Microenvironment

Principal Component Analysis¹
including all the Pre- and Post-treatment samples

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



NCT03799744 : Analysis of MoA in Clinical Samples

Perfusion changes induced by VCN-01

Dynamic contrast enhanced (DCE) were acquired from MRI images in Trial NCT03799744 (Systemic VCN-01 in HNSCC & Durvalumab¹)

Imaging biomarkers were obtained by a non-invasive imaging post-processing procedure. The delta (Δ) radiomic features for the lesions treated sequentially were extracted between the screening and the 1st follow-up (corresponding to week 8)

Radiomic markers suggest VCN-01 increases perfusion from the extravascular space to the intravascular space

K_{ep} marker
(rate transfer constant extravascular space \leftrightarrow blood)

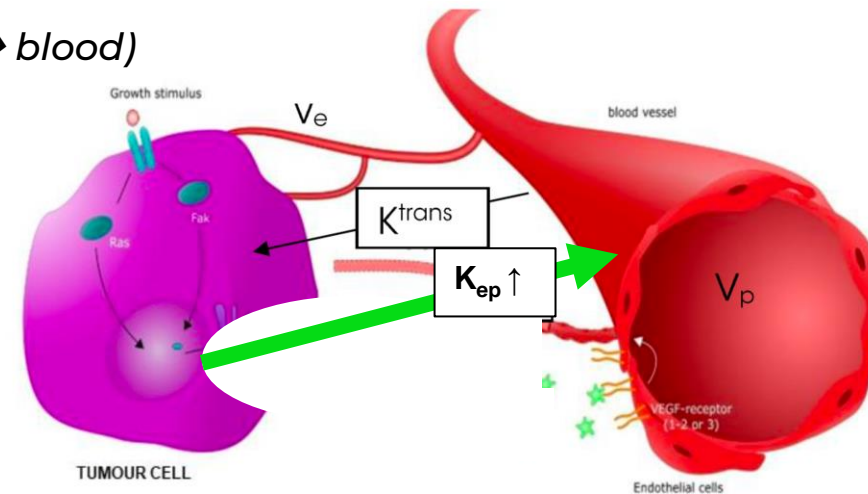
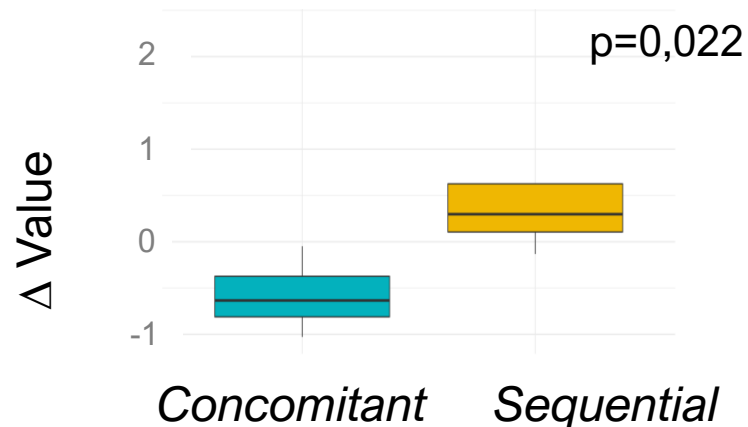


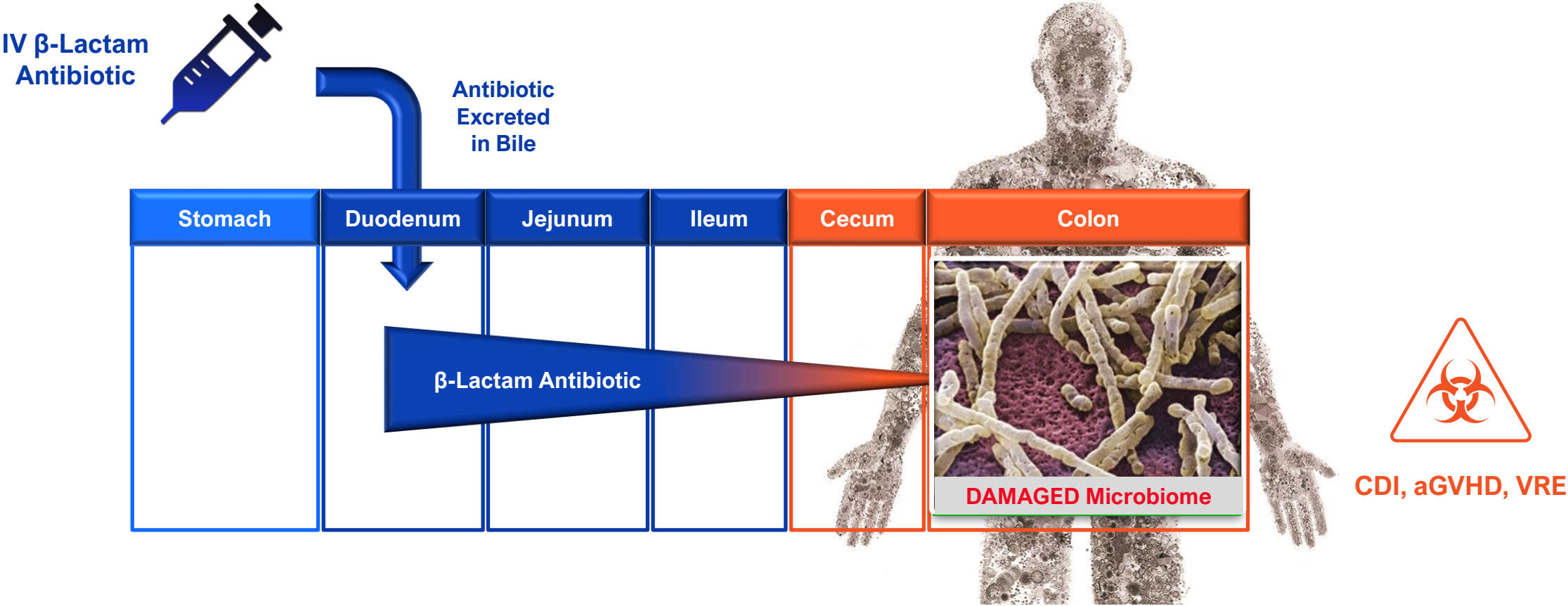
Figure 1. Pharmacokinetic perfusion model



SYN-004 (ribaxamase)

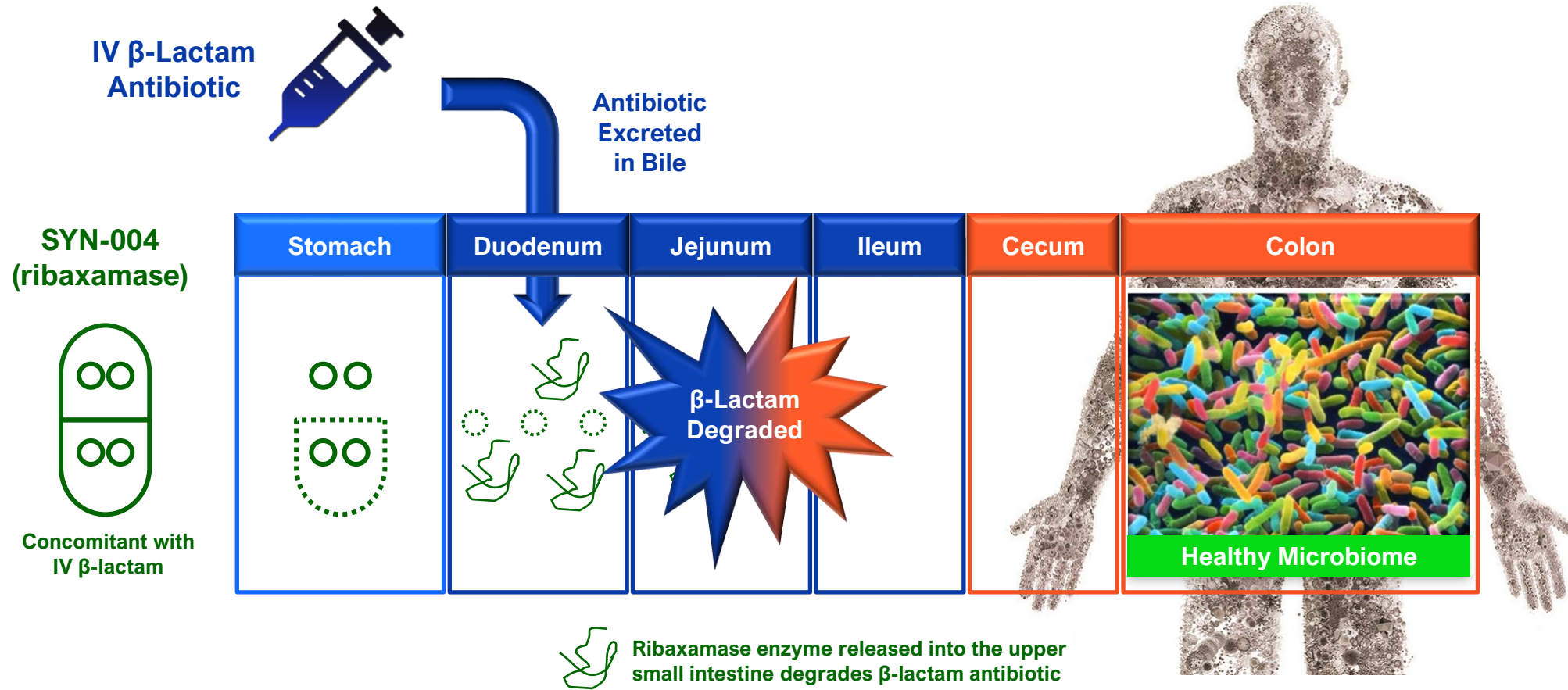
SYN-004 (ribaxamase) to Prevent Microbiome Damage

Antibiotics can damage the gut microbiome leading to disease

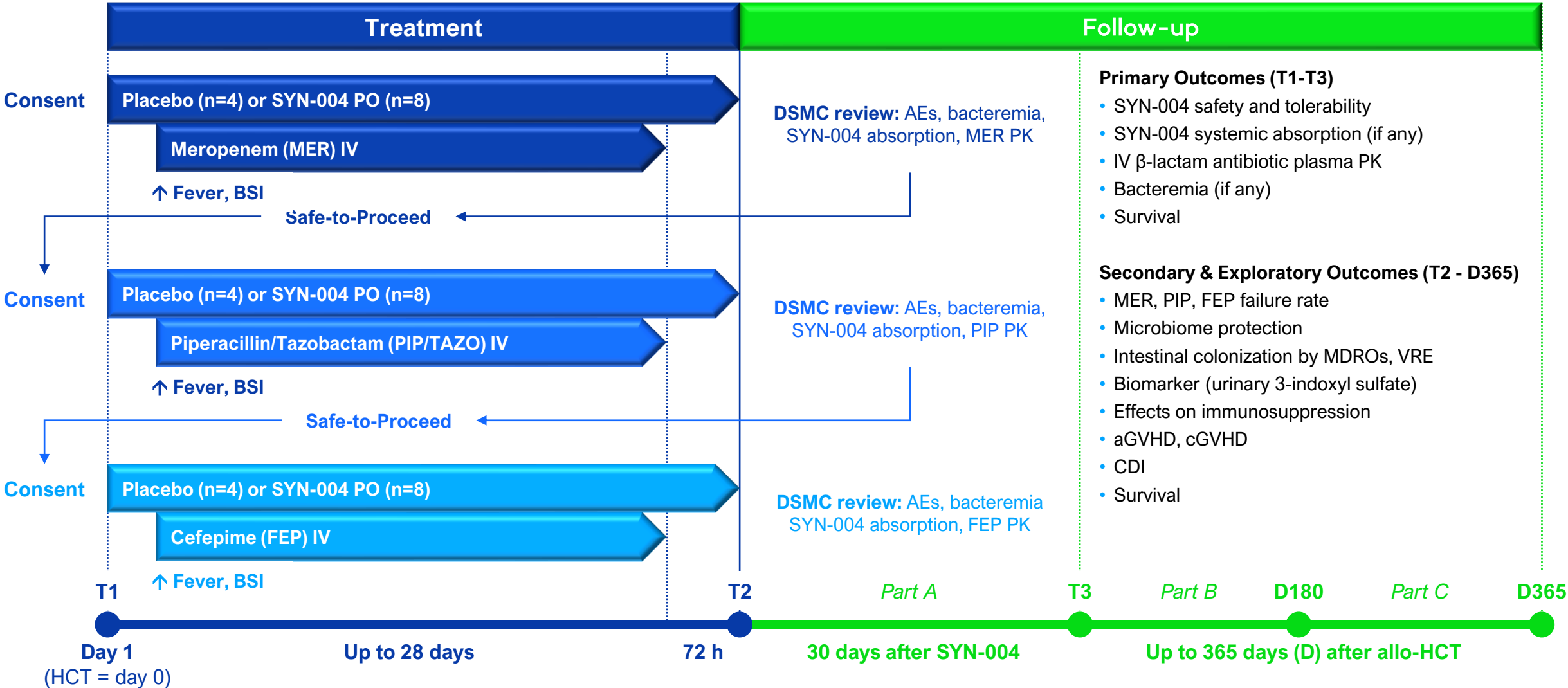


SYN-004 (ribaxamase) to Prevent Microbiome Damage

Preserving the gut microbiome to prevent disease



SYN-004 in Allo-HCT Patients Phase 1b/2a Study SB-1-004-006



SYN-004 in Allogeneic HCT Patients Study Update

- Completed Cohort 1 of 3 and proceeding to Cohort 2
 - 19 patients in Cohort 1 received at least one dose of study drug (SYN-004 or Placebo)
 - 16 patients received at least one dose of IV meropenem
 - 12 patients completed at least two meropenem PK periods and were evaluable towards the endpoints
- AEs and SAEs observed in Cohort 1 were typical for allo-HCT patients
 - AEs or SAEs were determined to be **unrelated** to study drug treatment by the investigators
 - A total of 29 severe TEAEs were reported among 12 participants (including 13 SAEs among 10 participants) most commonly infections/infestations including sepsis¹
- One patient died 14 days after the last dose of study drug due to sepsis that was unrelated to study drug²
 - Two patients died 72 days and 114 days after the last dose of study drug due to cancer relapse that was unrelated to study drug

SYN-004 in Allogeneic HCT Patients Study Update

- Consistent with studies in healthy volunteers, SYN-004 was not observed in plasma samples from the majority of patients
 - A total of 3 plasma samples had low but quantifiable SYN-004 levels (sensitive ECL assay)
 - No active SYN-004 enzyme was detected in these samples (functional activity assay)
- Meropenem pharmacokinetics were as expected for this patient population
 - Meropenem is not metabolized by SYN-004; PK sampling will be expanded in Cohorts 2 and 3
- DSMC convened on 20Sep2022 and recommended initiation of Cohort 2
 - Asked for more information about sepsis events but did not request protocol amendments
- Protocol amendment submitted to WU IRB 22Sep2022
 - Refine antibiotic PK sampling and monitoring of aGVHD prophylaxis/immunosuppressants
 - Assuming no IRB concerns, patient recruitment for Cohort 2 should start early Q4 2022



Corporate Summary

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)



Frank Tufaro PhD
Chief Operating Officer

Extensive executive experience, as well as clinical and academic experience in the development of oncolytic viruses based on herpes simplex and adenovirus, with numerous patents and peer-reviewed scientific publications



Vince Wachter PhD
Head Corporate Development

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

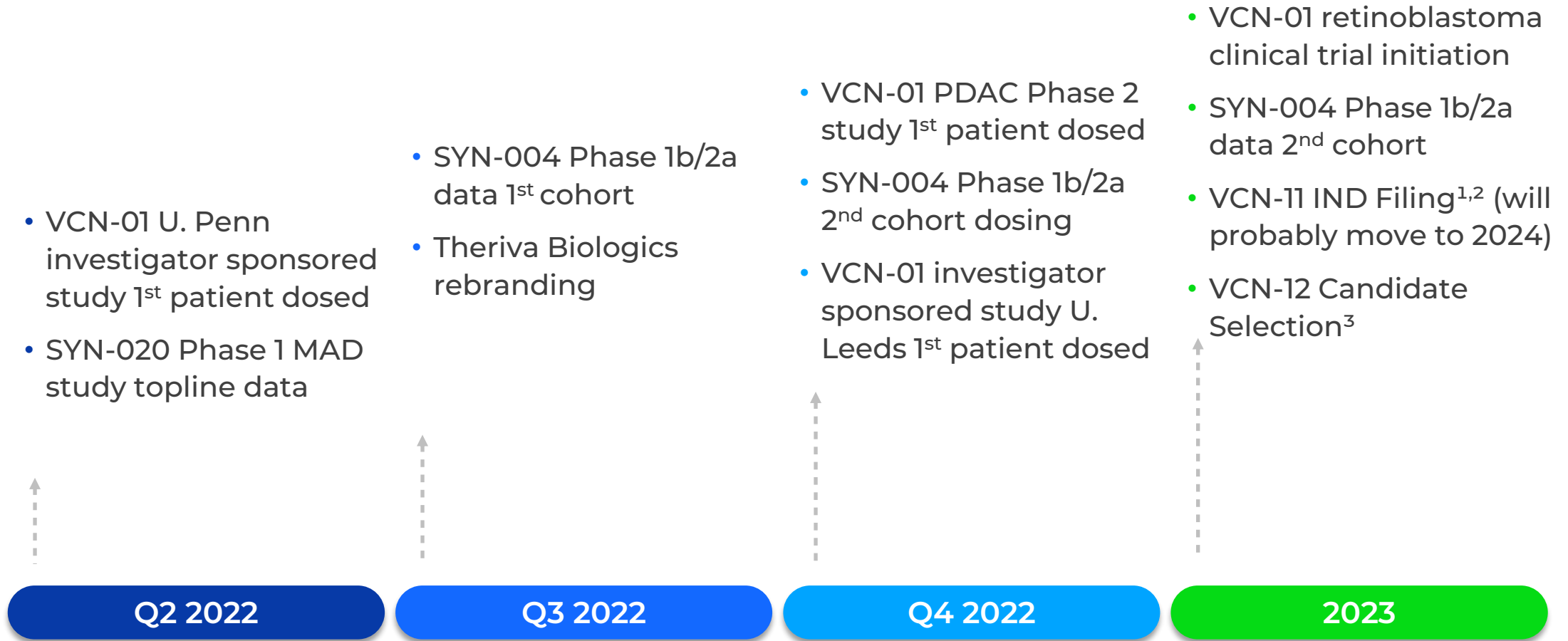
Development experience across oncology, infection, GI, metabolic diseases, transplantation, and drug delivery



Financial Snapshot

Exchange	NYSE American
Ticker	TVOX
Current Cash (as of 06/30/2022)	\$52.3 million
Average Daily Volume (3M Ave)	~195K
Locations	Rockville, MD Barcelona, Spain

Near-Term News Flow



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

Investment Highlights

Positioned at the forefront of oncolytic virus (OV) development

Unique, clinical-stage OV (VCN-01) optimized for systemic administration, selective tumor destruction, and enhancement of chemotherapy and immunotherapy

Expanding the pipeline with a next-generation OV that incorporates Albumin Shield™ technology (VCN-11) designed for hard-to-treat cancers

Multiple near-term catalysts

Lead product VCN-01 poised to enter a Phase 2 clinical study in metastatic pancreatic ductal adenocarcinoma and a Company sponsored study in retinoblastoma

Advancing SYN-004 in ongoing clinical trials

Accelerating the path to value

VCN-01 received Orphan Drug Designation (ODD) for retinoblastoma from the U.S. FDA and ODD by the EMA for pancreatic cancer

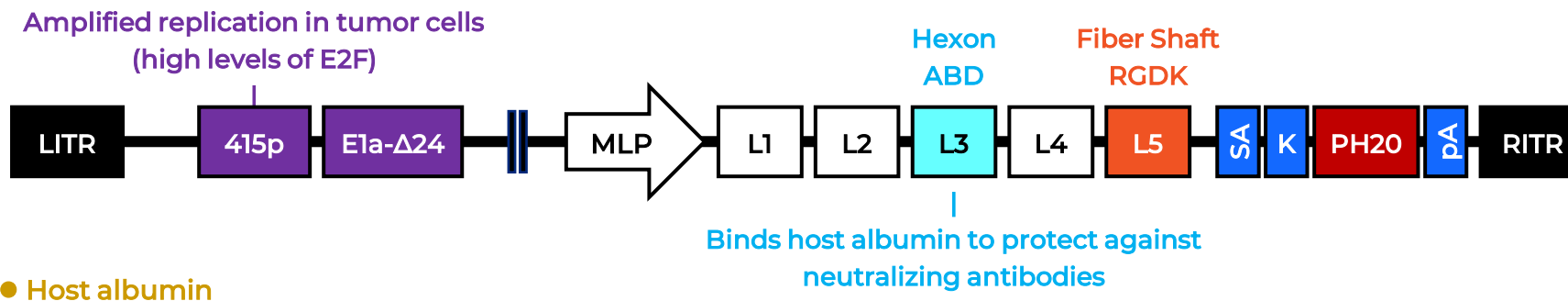
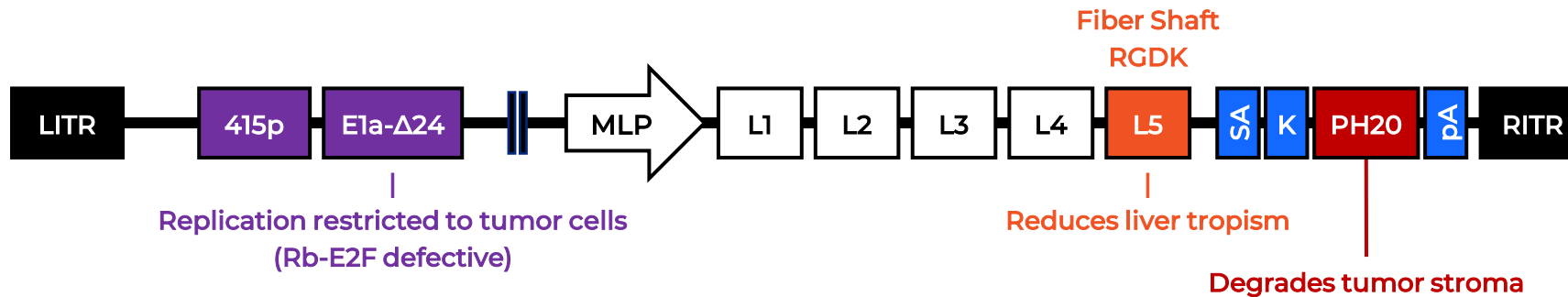
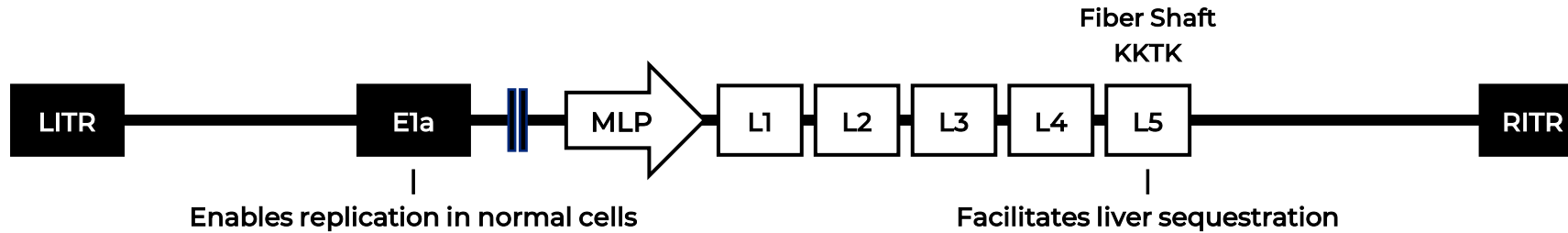
Established footprint in EU market for discovery and clinical development, partnering, and commercialization

Collaborations with leading research and academic institutions

Appendix



VCN Oncolytic Virus Genetic Modifications



ABD albumin binding domain (streptococcal protein G)¹

Ad5 Adenovirus type 5

E1a-Δ24 deletion of 24 base pairs within the E1a promoter; further modified by insertion of 8 extra E2F binding sites and one Sp1-binding site at nucleotide site 415 (**415p**)

MLP major late promoter²

PH20 soluble human testicular hyaluronidase³

KKTK Lys-Lys-Thr-Lys putative HSPG binding domain on fiber shaft

RGDK Arg-Gly-Asp-Lys inserted in place of KKTK on fiber shaft

VCN-12 VCN-11 armed with additional therapeutic transgene

VCN 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 2019, 29 September 2019, Barcelona, Spain. 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 2019, 28 September 2019, Barcelona, Spain.
- 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
- Sarantis P et al. (2020) Pancreatic ductal adenocarcinoma: treatment hurdles, tumor microenvironment and immunotherapy. *World J Gastrointest Oncol* 12:173-181
- 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.
- 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>
- Ushio J et al. (2021) Pancreatic ductal adenocarcinoma: epidemiology and risk factors. *Diagnostics* 11:562

TREATMENT

- 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

Retinoblastoma 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