

2023 Annual Shareholder Meeting

Wednesday, June 21st



Forward-Looking Statements

The information in this presentation may include "forward-looking statements," within the meaning of U.S. securities legislation, relating to the business of Provectus Biopharmaceuticals, Inc. and its affiliates (Provectus or the Company), which are based on the opinions and estimates of Provectus management and are subject to a variety of risks and uncertainties and other factors that could cause actual events or results to differ materially from those projected in the forward-looking statements. Forward-looking statements are often, but not always, identified by the use of words such as "seek," "anticipate," "budget," "plan," "continue," "estimate," "expect," "forecast," "goal," "may," "will," "project," "predict," "potential," "targeting," "intend," "could," "might," "should," "believe," and similar words suggesting future outcomes or statements regarding an outlook.

The safety and efficacy of the agents and/or uses under investigation have not been established. There is no guarantee that the agents will receive health authority approval or become commercially available in any country for the uses being investigated or that such agents as products will achieve any particular revenue levels.

Due to the risks, uncertainties, and assumptions inherent in forward-looking statements, readers and listeners should not place undue reliance on these forward-looking statements. The forward-looking statements contained in this presentation are made as of the date hereof or as of the date specifically specified herein, and the Company undertakes no obligation to update or revise any forward-looking statements, whether as a result of new information, future events or otherwise, except in accordance with applicable securities laws. The forward-looking statements are expressly qualified by this cautionary statement.

Forward-looking statements are subject to risks, uncertainties, and assumptions, many of which relate to factors beyond Provectus's control. Risk, uncertainties, and assumptions include those discussed in the Company's filings with the U.S. Securities and Exchange Commission (SEC), including those described in Item 1A of Provectus's:

- Report on Form 10-K for the year ended December 31, 2022, and
- Report on Form 10-Q for the quarter ended March 31, 2023.



2023 Annual Shareholder Meeting Agenda

Part 1: Shareholder Meeting Activities

- 1. Welcome
- 2. Introductions
- 3. Preliminary Matters
- 4. Order of Business
- 5. Other Business
- 6. Report of the Inspector of the Election
- 7. Conclusion of the Meeting

Part 2: Company Update

- A. Opening Remarks
- B. Presentation: Provectus's Next Chapter
- C. Q&A Session
- D. Closing Comments

Part I: Shareholder Meeting Activities





Shareholder Meeting Activities

- 1. Welcome
- 2. Introductions
- 3. Preliminary Matters
 - Inspector of the Election
 - Record Date
 - Shares Entitled to Notice and Vote
 - Quorum
 - Reading of the Notice of the Meeting, Affidavit of Mailing, and Minutes
 - Stockholders' Proxies
 - Stockholders' Ballots

4. Order of Business

Proposal #1: To elect five directors to serve on our Board of Directors

Proposal #2: To conduct an advisory vote to approve the compensation of our named executive officers

Proposal #3: To approve, on an advisory basis, the frequency of the advisory vote on the compensation of our named executive officers

Proposal #4: To ratify the selection of Marcum LLP as our independent registered public accounting firm for 2023

Proposal #5: To authorize our Board of Directors to amend our Certificate of Incorporation, as amended by the Certificate of Designation of Series D Convertible Preferred Stock and Certificate of Designation of Series D-1 Convertible Preferred Stock, to effect a reverse stock split of our common stock, Series D Convertible Preferred Stock, and Series D-1 Convertible Preferred Stock at a ratio between 1-for-10 and 1-for-50, where the ratio would be determined by our Board of Directors at its discretion, and to make corresponding amendments to the Certificates of Designation to provide for the proportional adjustment of certain terms upon a reverse stock split

Proposal #6: To authorize our Board of Directors, if and only if Proposal #5 is approved, to amend our Certificate of Incorporation, as amended by the Certificates of Designation, to decrease the number of authorized shares of our common stock and preferred stock by the same reverse stock split ratio determined by our Board of Directors

- 5. Other Business
- 6. Report of the Inspector of the Election
- 7. Conclusion of the Meeting

Part 2: Company Update





Opening Remarks

Ed Pershing, CPA, Chair, Board of Directors



Provectus's Next Chapter

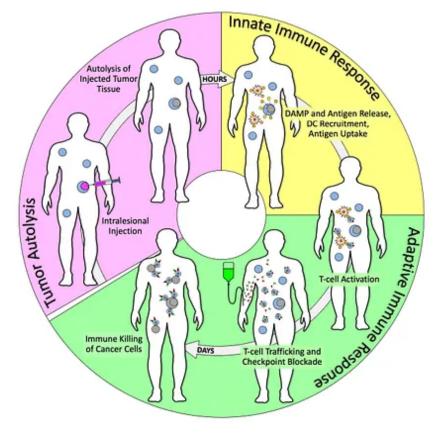
Dominic Rodrigues, Vice Chair, Board of Directors



PV-10 (rose bengal sodium; RBS): Cancer Immunotherapy for Injectable Solid Tumors

- o Cancer immunotherapy agnostic to tumor type
- Small molecule drug product candidate injected into tumors on/inside the body
- o 3-step, multi-variate, interconnected & interrelated systemic mechanism
 - Within hours of PV-10-injection: Tumor tissue cell death
 - Innate immune signaling from the release of DAMPs, tumor antigens,
 cytokines, etc. from PV-10-injected tumors
 - Within days of PV-10 injection: Tumor-specific functional T cell response
- 450+ patients treated: 15+ multi-country, early-to-late-stage trials, distinct cohorts, expanded access programs, and QoL studies: melanoma, NMSCs, HCC, liver metastases (colorectal, uveal, pancreatic, others), and breast cancer
 - <u>25+ journal publications</u>; <u>50+ medical conference presentations</u>¹
- Skin, liver, and breast cancers represent ~20% of 2023 estimated U.S.
 incidences of solid tumor disease

Figure 1. PV-10 Immuno-Oncology Cycle²



^{*} DAMP = damage-associated molecular pattern. QoL = quality of life. NMSC = non-melanoma skin cancer. HCC = hepatocellular carcinoma. 1 AACR, ASCO, CIO, ECC, ENETS, ESMO, ESMO GI, ESMO IO, ISOO, Melanoma Bridge, SIR, SITC, SMR, SSO, etc. 2 Maintains the involvement of immune checkpoint blockade (i.e., green-colored intravenous bag) for medical combination and business rationales.





Figure 2.

Single-Agent Treatment Cutaneous/Subcutaneous Tumors

Phase 1 Metastatic Melanoma

Phase 2 Metastatic Melanoma

Phase 3 RCT Locally Advanced Cutaneous Melanoma¹

> Phase 1 Breast Cancer

Intermediate-Size Expanded Access: Cu/Subcu Tumors

- Australia (publications: 3 sites)
- USA

QoL Study Locally Advanced Cutaneous Melanoma Single-Agent Treatment
Visceral Hepatic
Tumors

Phase 1 Cancers of the Liver

- HCC; Colorectal cancer (mCRC)
- · Pancreatic cancer
- · Uveal melanoma (mUM)
- Other tumor types (4+)

Phase 1
Metastatic
Neuroendocrine Tumors

Combination Therapy
Cutaneous/Subcutaneous &
Visceral Tumors

Phase 1b Cutaneous Melanoma

- +Keytruda®
- Checkpoint-naïve Stage IV
- Checkpoint-refractory Stage IV
- · Checkpoint-naïve Stage III

Phase 1 Metastatic Uveal Melanoma

- +Keytruda
- +Yervoy®+Opdivo®

Single-patient Expanded
Access:
Cu/Subcu Tumors

· Multiple settings, USA

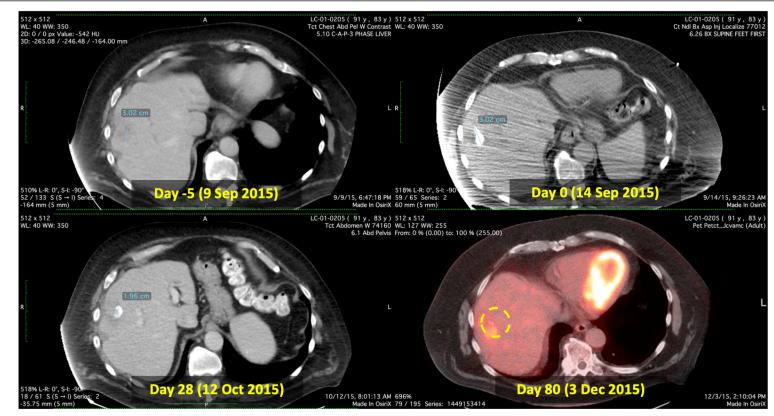
Historical process/data gaps highlighted the need for:

- 1. Optimized PV-10 pharmacokinetics (PK)
- 2. Well understood, clearly defined, target patient populations
- 3. Study EPs unequivocally supportive of clearlydefined trajectories along potential regulatory pathways
- 4. Well-established, well-reasoned, functional EP measurement
- 5. Comprehensive immune correlative assessment undeniably demonstrating immunotherapeutic outcomes largely due to PV-10 treatment
- Compelling clinical-business rationales sufficiently addressing SOC, potential regulatory pathways, and/or commercial development

This knowledge organizes the settings for comparing PV-10-led treatments to actual or historical SOCs to assess clinical benefit (Part Two of Provectus's clinical development program for PV-10)

^{*} Cu/Subcu = cutaneous/subcutaneous. RCT = randomized controlled trial. HCC = hepatocellular carcinoma. mCRC = metastatic colorectal cancer. mUM = metastatic uveal melanoma. EP = endpoint. SOC = standard of care. ¹ Terminated.

"Poster #1." Internal 2015: Single-Agent PV-10 for Visceral Hepatic Tumors (Pancreatic Cancer)

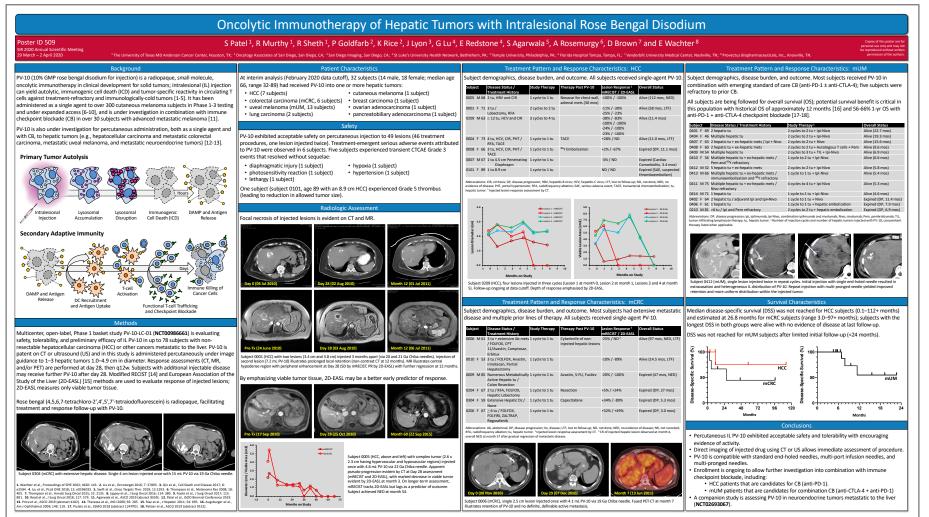


- Male, age 83, BMI 34.4, with moderately to poorly differentiated adenocarcinoma of pancreatobiliary origin (occult primary)
- Presented with two hepatic metastases, 3.3 and 4.7 cm (17 Jun 2015)
- 3.3 cm lesion injected once with 9.0 mL PV-10 (14 Sep 2015) as first-line monotherapy
- Retention of PV-10 evident at Day 28 and Day 80 (minimal PET avidity of injected lesion at Day 80 Final study radiology)
- Gradual progression of existing disease evident throughout 2016 without new lesions
- Declined starting systemic chemotherapy at Month 17 and lost to follow-up
- Overall survival 29 months from PV-10 administration (expired from disease progression)

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Poster #2. SIR 2020: Single-Agent PV-10 for Visceral Hepatic Tumors (HCC, mCRC)



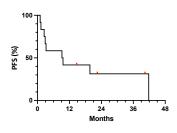
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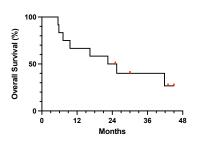
^{*} SIR 2020 ePoster Gallery of the canceled Society of Interventional Radiology (SIR) 2020 Annual Scientific Meeting: Oncolytic immunotherapy of hepatic tumors with intralesional rose bengal disodium.

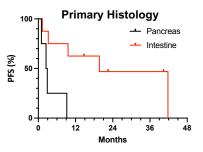


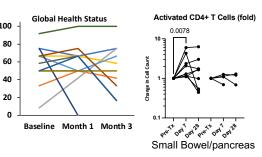
Poster #3. ENETS 2022: Single-Agent PV-10 for Visceral Hepatic Tumors (mNET)

Secondary endpoints: PFS, overall survival and OOL









Median PFS 9.4 months

• Range 1.0 to 41.8 months

Median OS 22.5 months

- Range 5.5 to 42.3 months (4 subjects alive) Median OS 11.8 mon vs 25.5 mon
- Median PFS 2.7 mon vs 19.7 mon

Conclusion

- PV-10 elicited no safety concerns and multiple doses were safely delivered.
- Encouraging evidence of both local and systemic disease and symptom control was seen in a heavily pretreated population.
- PV-10 may be an option for patients who have failed standard therapy.
- Combining PV-10 with systemic checkpoint inhibitors may enhance the proposed immune mechanism.
- Non-clinical data in other poorly immunogenic tumour types suggests PV-10 may enhance activity of cytotoxic therapies, such as PRRT.

19th Annual ENETS Conference | 10 – 11 March 2022

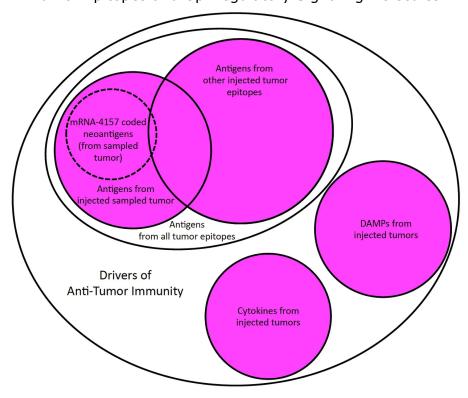
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^{* 2022} annual conference of the European Neuroendocrine Tumor Society (ENETS): Phase 1 study of Intralesional (IL) rose bengal (PV-10), an investigational autolytic immunotherapy

Part One Knowledge (illustrative)

- o RBS is an immuno-catalyst small molecule
- o PV-10 is a cancer immunotherapy agnostic to tumor type
 - Tumor-specific
 - Stimulatory + Inhibitory
 - Multiple, independent, temporally-activated signaling pathways (2011); e.g.:
 - Lysosomal targeting (2002, 2019) [stimulatory]
 - STING (2020) [stimulatory]
 - WNK-1/β-Catenin (2022) [inhibitory]
 - LAMP-2 (2023) [inhibitory]
 - Proprietary (ongoing)
- o 3-step, multi-variate, interconnected & interrelated systemic mechanism
 - Tumor autolysis
 - Innate immune response
 - Adaptive immune response
- Each PV-10-injected tumor is a library of germane information for the immune system, producing antigens:
 - Present in each injected tumor of the patient (i.e., the patient's libraries of their cancer data)
 - Specific to each injected tumor
 - And multiple co-stimulatory factors, such as DAMPs
 - From within the TME, because PV-10 is injected directly into the TME itself
- o Synergy and orthogonality (mechanism; activity; safety) with SOC medicines

Figure 3. PV-10 Induces Adaptive Immunity via Synchronous Release of Tumor Antigens from All Injected Tumor Epitopes and Up-Regulatory Signaling Molecules



Outcome: Medical science-driven confidence of Phase Two clinical development program design and patient outcomes

^{*} TME = tumor microenvironment. Right image contrasts and compares PV-10 and investigational cancer vaccine mRNA-4157. See May 15th Provectus Substack post Cancer immunotherapy PV-10's evolution into a cancer immunotherapy.



Provectus's Clinical Study Design Principles for PV-10

A) Optimized PV-10 pharmacokinetics

- PV-10 PRN
- Treat and retreat baseline disease and new lesions over time

B) Well understood, clearly defined, target patient population

- Single-agent PV-10 may have a distinct, influential impact on untreated metastatic disease
- Target solid tumor cancers where mOS is low and, for now, where checkpoint does not work in 1st-line but could in 2nd-line with PV-1

C) Study EPs unequivocally supportive of a clearly-defined trajectories along potential regulatory pathways

• Overall patient CR or mCR may be prognostic of OS, and thus could be prognostic of PFS (i.e., a faster time-to-event EP)

D) Well-established, well-reasoned, functional EP measurement

- Treat and retreat baseline disease and new lesions prior to first RECIST measurement
- Maximize first observation-of-progression period (i.e., first RECIST measurement) that is also acceptable to RECIST
- Visceral disease: measure response using PERCIST to determine if mCR has been achieved; correlate RECIST ORR and PFS outcomes with potential PERCIST mCR outcomes

E) Comprehensive immune correlative assessment undeniably demonstrating an immunotherapeutic outcome largely due to PV-10 treatment

- PV-10 facilitates a specific innate immune response via DAMP release
- PV-10 activates a specific adaptive response via a functional T cell response

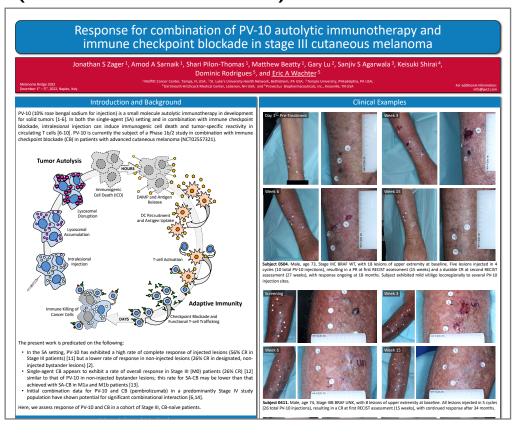
F) Compelling clinical-business rationale sufficiently addressing SOC, potential regulatory pathways, and/or commercial development

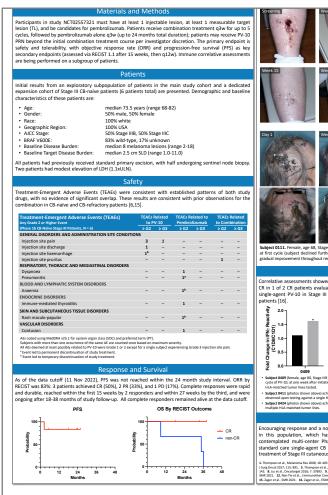
• See Slide #19

^{*} PRN = pro re nata or as needed. mOS = median overall survival (OS). CR = complete response. mCR = metabolic CR. RECIST = Response Evaluation Criteria in Solid Tumors. PERCIST = Positron Emission Tomography Response Criteria in Solid Tumors. ORR = objective response rate. PFS = progression-free survival. See May 15th Provectus Substack post Cancer immunotherapy PV-10's evolution into a cancer immunotherapy.



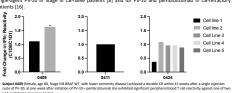
Poster #4. Melanoma Bridge 2022: PV-10 Combination Therapy for Cutaneous Tumors (Cutaneous Melanoma)







Correlative assessments showed increased T cell reactivity to HLA-matched tumor that preceded a durable CR in 1 of 2 CR patients evaluated for this biomarker. Similar immune upregulation has been shown with single-agent PV-10 in Stage III CB-naive patients [8] and for PV-10 and pembrolizumab in CB-refractory



Subject DR11 (photos shown above) achieved a durable CR within 15 weeks upon repeat intervention with PV-10; T cell reactivity was not-observed upon testing against a single H-1 machiest humor line.
 Subject DR22 (photos shown above) achieved a PR after a single intervention with PV-10; T cell reactivity was not observed upon testing against minks of the company of the cell of the cell

Encouraging response and a non-overlapping safety profile support further evaluation of the combination in this population, which has previously exhibited suboptimal response to single-agent CR, via a contemplated multi-center Phase 2 randomized controlled trial of PV-10 and investigator's choice of standard care single-agent CB versus investigator's choice of standard care single-agent CB for first-line treatment of Stage III cutaneous melanoma.

L Thompson et al., Melanoma Nas 2000; 18-65. 2. Thompson et al., Annali Sung Orea 2015; 22: 2115. 3. Uppey et al., 15up Orea 2016; 114-100. 4. Hones et al. 15up Orea 2015; 115: 201. 4. Uppey et al., 15up Orea 2016; 114-100. 4. Hones et al., Note 2017; 112: 201. 4. Aprenalis et al., 1500 0. 2017. 7. Welcher et al., Proceedings of PRE 2002; 45: 0. 45:

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Optimized PV-10

^{*} Melanoma Bridge 2022: Response for combination of PV-10 autolytic immunotherapy and immune checkpoint blockade in stage III cutaneous melanoma



Poster #5. ASCO 2022: PV-10 Combination Therapy for Visceral Hepatic Tumors (mUM)



Metabolic complete responses in metastatic uveal melanoma patients treated with image-guided injection of PV-10

Krysta McVay¹, Rahul Sheth¹, Ravi Murthy¹, Dan S. Gombos1, Brett Carter¹, Priya Bhosale¹, Nourel Hoda Tahon¹, Gener Balmes¹, Ysabelle Coz¹, Edwina Washington¹, Dominic Rodrigues², Eric Wachter², Sapna P. Patel¹

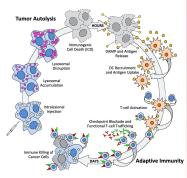
MDAnderson Cancer Center

Abstract #9543

11 (19%) 20 (34%)

Background

Rose bengal disodium (PV-10) is a small molecule oncolytic immunotherapy in clinical development for treatment of solid tumors [1-4]. When administered by intralesional injection. PV-10 can produce an immunogenic cell death that may induce a T-cell mediated immune response against treatment-refractory and immunologically-cold tumors [5-8]. Adaptive immunity can be enhanced through combination with immune checkpoint blockade (CB) [4,8].



Traditional CT imaging can underestimate the degree of anti-cancer treatment effect due to reliance on morphological changes of visualized tumors. In contrast, PET imaging offers information on metabolic activity using a positron-emitting radiolabeled agent (e.g. FDG) but is less sensitive to changes in tumor size. FDG-PET images acquired, co-registered, and superimposed on CT images (PET-CT) allow spatial detection of anti-cancer activity. Moreover, FDG-PET-CT can provide information regarding anti-tumor immune responses in patients receiving immunotherapy

Response assessment of injected lesion response by RECIST and 2D EASL [9] criteria allows evaluation of PV-10 treatment effect and may provide early prognostic evidence of potential clinical benefits of metabolic complete response (mCR) and overall survival (OS).

Methods

¹The University of Texas MD Anderson Cancer Center, ²Provectus Biopharmaceuticals

PV-10-LC-01 (NCT00986661) is an open-label Phase 1 study evaluating the safety, tolerability, and preliminary efficacy of intralesional PV-10 in patients with solid tumors metastatic to the liver. PV-10 is administered percutaneously to 1-3 designated hepatic tumors 1.0-4.9 cm in diameter. Response assessments are performed at Day 28, then every 3 months, Patients with additional injectable tumors may receive further PV-10 after Day 28. Here we describe the experience in a cohort of patients with metastatic uveal melanoma (mLIM). Fligible nationts could receive standard of care CB during or after PV-10

Patient Characteristics

All patients had at least 1 injectable hepatic metastasis; approximately half had additional extra-hepatic disease Seven patients underwent PET-CT during the study; 4 achieved mCR (including 2 patients with extensive extrahepatic disease). mCR patients were similar to the general study population, with the exception of a lower overall M-category, and received similar study treatment.

Table 1. Patient characteristics and study treatment

Category	All Patients (N)	mCR Patients (N)
No. Patients	23	4
Age, median (range)	64 (32-80)	68 (56-70
Gender		
Male	12	2
Female	11	2
M-category		
M1a (largest diameter ≤ 3.0 cm)	14	4
M1b (largest diameter 3.1–8.0 cm)	8	0
M1c (largest diameter ≥ 8.1 cm)	1	0
Sites of metastatic disease		
Hepatic only	12	2
Hepatic + extra-hepatic	11	2
Prior lines of therapy		
0	10	2
1	11	1
2+	2	1
Prior treatment		
Immunotherapy	12	2
No immunotherapy	11	2
Study treatment		
PV-10 only	6	1
PV-10 + PD-1	6	0
PV-10 + PD-1 + CTLA-4	11	3
PV-10 treatment cycles, median (range)	2.0 (1-6)	1.5 (1–3)
Lesions injected, median (range)	2.0 (1-11)	2.0 (1-3)

Lesion response

Equivalent response patterns were observed when injected lesions were assessed via CT using RECIST and 2D EASL criteria. Patients achieving mCR generally exhibited stabilization or regression of their injected lesions, but did not achieve CR by CT, with maximum response developing gradually.

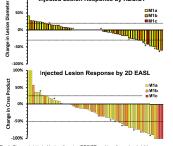


Fig. 1 Change in injected lesion diameter (RECIST) and two dimensional viable cross product (2D EASL). Asterisks indicate response of lesions in patients achieving mCR. Dashed horizontal lines denote response thresholds for the respective assessment criter

(Injected Lesions)

Objective responses

No. Lesions Evaluated

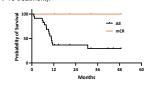
11 (19%)	16 (28%)
39 (66%)	30 (52%)
9 (15%)	8 (14%)
due to a baseline cross p	roduct of zero.
12 18	
	39 (66%)

Fig. 2 Change in injected lesion diameter (RECIST); orange lines illustrate pachieving mCR compared to the general study population (grey bars).

Survival

Median OS was 10.7 months (range 1.1 to 48.8+ months) from initiation of PV-10 treatment; OS from the onset of metastatic disease was 16.9 months (range 2.7 to 72.2+ months)

All four patients achieving mCR were alive at data cutoff (range 12.4+ to 48.8+ months from initiation of



Safety

Acceptable safety was observed with no mortality or permanent Grade 3 or higher morbidity attributed to study treatment.

Conclusions

- PV-10 can induce mCR in both injected (adscopal) and non-injected (abscopal) lesions.
- mCR suggests immunogenic cell death in mUM patients with liver metastases.
- CT response assessment may underestimate the effect of PV-10 in injected tumors; 2D EASL is more sensitive than RECIST to changes in injected lesions, but both are less sensitive than PET-CT.
- Translational research is underway to elucidate the molecular basis for mCR responders vs nonresponders

References

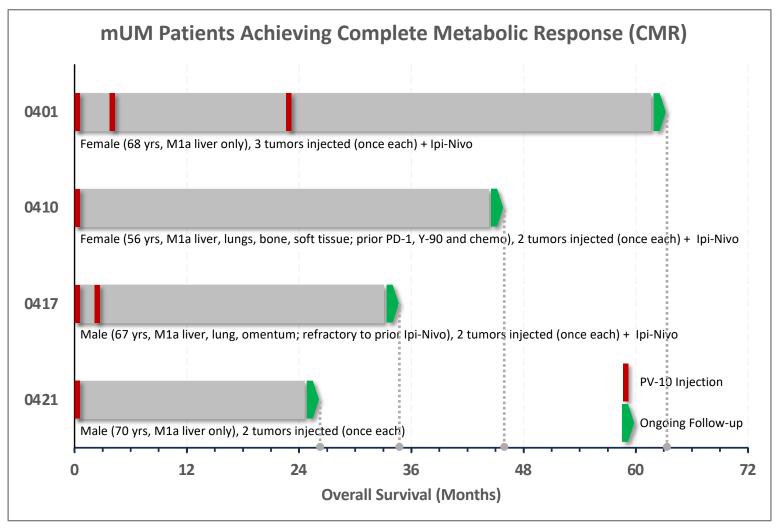
- Thompson et al., Annals Surg Oncol 2015; 22: 2135.
- Transpool et al., Anihans Surg (Intick 2016, 22, 2)33. Patile et al., 1820 20 (abstract to 1509). Price et al., ASCP 2020 (abstract et 16084). Yeager et al., SIMR 2021. Warchier et al., Proceedings of SPIE 2002, 4620: 143. Liu et al., Orcharget 2016; 7: 3783. On et al., Cell Death and Disease 2017; 8: e2584. Liu et al., PLO NE 2016; 13: e0196033.
- Riaz et al., J Hepatol. 2011; 54: 695.

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^{* 2022} American Society of Clinical Oncology (ASCO) annual meeting: Metabolic complete responses (mCR) in metastatic uveal melanoma (mUM) patients treated with image-guided injection (IGI) of PV-10



"Poster #6." Internal 2023: PV-I0-Led Therapy for Visceral Hepatic Tumors (mUM)



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- Patient 0401 had 3 tumors injected, once each, in 3 sequential PV-10 treatment cycles
- ⇔ 0410 had 2 tumors injected in a single PV-10 treatment cycle
- ⇔ 0417 had 2 tumors injected, once each, in 2 sequential PV-10 treatment cycles
- □ 0421 had 2 tumors injected in a single PV-10 treatment cycle

^{*} CMR is the same as mCR. Patient demographics: Single-agent PV-10, PV-10 combination therapy (+Yervoy [ipi]+ Opdivo [nivo]); checkpoint-naïve, checkpoint-refractory; hepatic disease only, hepatic & extrahepatic disease.



Part Two of Provectus's Clinical Development Program for PV-10

1) The combination of PV-10 and poly-chemotherapy for FOLFIRINOX-refractory pancreatic cancer metastatic to the liver (NEW)

- Phase 1; 2nd-line setting; PV-10+gemcitabine (gem)+nab-paclitaxel (nab)
- Primary EPs: Safety and tolerability, OS; Secondary EPs: Overall patient CR & ORR and PFS (RECIST), mCR (PERCIST)
- Historical control arms: 1st-line setting—gem+nab = mOS of 8.5 months (Von Hoff et al. 2013), FOLFIRINOX = mOS of 11.1 months (Conroy et al. 2011); 2nd-line gem+nab refractory to FOLFIRINOX = mOS of 6.6 months (Huffman et al. 2023)
- Will the data support the contention that PV-10 is a cancer immunotherapy? Can 2nd-line PV-10 combination therapy beat 1st- and 2nd-line SOC mOS?

2) The combination of PV-10 and SOC checkpoint for checkpoint-naïve Stage III cutaneous melanoma (CONTINUATION)

- Phase 2 RCT; 1st-line setting; PV-10+SOC checkpoint vs. SOC checkpoint (actual control arm)
- Primary EP: Overall patient CR (RECIST); Secondary EPs: Overall patient ORR and PFS (RECIST), OS
- Will the data support, among other things, that PV-10 combination therapy CR > single-agent SOC checkpoint ORR?

3) The combination of PV-10 and immunotherapy or dual checkpoints for treatment-naïve, M1a-staged mUM (CONTINUATION)

- Phase 1+; Prospective 1st-line setting; PV-10+ipilimumab (ipi)+nivolumab (nivo)
- EPs: OS, Overall patient CR & ORR (RECIST), mCR (PERCIST), PFS (RECIST)
- Historical M1a-staged control arms: 1st-line setting—Kimmtrak® (tebentafusp; HLA-A*02:01-positive) = mOS of TBD months (Nathan et al. 2021), ipi+nivo = mOS of 13.9 months (Pelster et al. 2021)
- Will the data support that PV-10 combination therapy mOS for M1a patients > SOC mOS? What is the rate of PV-10 combination therapy mCR?

Clinical strategy: Leverage PV-10's immunotherapeutic traits and effect size to assess clinical benefit (e.g., response, durability, survival, etc.) by comparing PV-10-led treatments and actual/historical SOCs in all Part Two studies

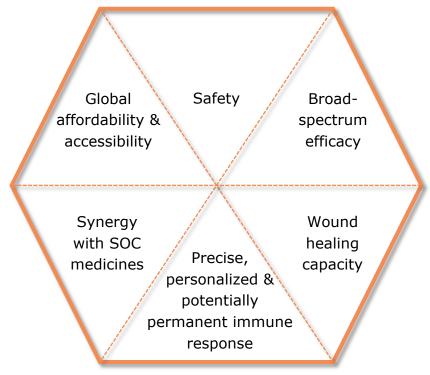
^{*} FOLFIRINOX = Leucovorin Calcium (Folinic Acid) (FOL)+Fluorouracil (F)+Irinotecan Hydrochloride (IRN)+Oxaliplatin (OX). See May 15th Provectus Substack post Cancer immunotherapy PV-10's evolution into a cancer immunotherapy.



Provectus's Rose Bengal Sodium (Halogenated Xanthene) Medical Science Platform

- o Clinical development programs
 - Oncology (intratumoral)
 - Dermatology (topical)
 - Ophthalmology (topical)¹
- o *In vivo* proof-of-concept programs
 - Oncology (oral)
 - Hematology (oral)
 - Wound healing (topical)
 - Animal health (intratumoral; canine solid tumor cutaneous cancers)
- o *In vitro* preclinical discovery programs
 - Infectious diseases
 - Tissue regeneration and repair

Figure 5. RBS Medical Science-Driven Value Proposition



Business goal: Demonstrate the potential of pharmaceutical-grade RBS-formulated drug product candidates for different diseases

¹ In collaboration with Bascom Palmer Eye Institute.



Provectus's Pharmaceutical-Grade Rose Bengal Sodium Drug Substance Manufacturing

- o Pharmaceutical-grade RBS results from, among other things:
 - Proprietary, patented, commercial-scale processes to synthesize and utilize the RBS molecule into a viable API for commercial pharmaceutical use
 - Development of unique chemistry, manufacturing, and control (CMC) specifications for drug substance (DS) and drug product (DP) candidate manufacturing processes
 - Production and multi-year stability testing of multiple RBS DS and PV-10 DP candidate lots
 - · Comprehensive documentation of lot composition and reproducibility
 - Review and acceptance of CMC data from these lots by 7 different national drug regulatory agencies for use in Provectus's prior Phase 3 RCT¹
- RBS DS and PV-10 DP candidate manufacturing processes employ Quality-by-Design (QbD) principles, current Good Manufacturing Practice (cGMP) regulations, and The International Council for Harmonization (ICH) of Technical Requirements for Pharmaceuticals for Human Use guidelines
 - These processes utilize controls that eliminate the formation of historical impurities and avoid the introduction of hazardous impurities present in uncontrolled and unreported amounts in non-pharmaceutical-grades of rose bengal
- Non-pharmaceutical-grades of rose bengal suffer from the uncontrolled presence of substance-related impurities and/or gross contaminants, substantial lot-to-lot manufacturing variability, inaccurately reported purity and contents, and the lack of reproducible, consistent, and fulsome CMC specifications and documentation (see bullet #10 on Slide #24)

Figure 4. Trademark for Provectus's Process to Synthesize the RBS Molecule into an API for Pharmaceutical Use



Business goal: Establish the commercial differentiation, viability, and scale of pharmaceutical-grade RBS DS and RBS DS-based DP candidates

^{*} API = active pharmaceutical ingredient. ¹ Provectus's processes of synthesizing the RBS molecule into pharmaceutical-grade RBS and manufacturing RBS DS and PV-10 DP candidate, the processes' CMC specifications, and the CMC data from the production of stability lots of DS and DP were reviewed by the U.S. Food and Drug Administration (FDA), Germany's Bundesinstitut für Arzneimittel und Medizinprodukte (BfArM), Australia's Therapeutic Goods Administration (TGA) under a clinical trial notification, France's Agence Nationale de Sécurité du Médicament et des Produits de Santé (ANSM), Italy's Agenzia Italiana del Farmaco (AIFA), Mexico's Comisión Federal para la Protección contra Riesgos Sanitarios (COFEPRIS), and Argentina's Administración Nacional de Medicamentos, Alimentos y Tecnología Médica (ANMAT).



2022-2023 Presentations, Publications, Patents, and Other Company Achievements*

- **1. July 2022.** Initiated a new sponsored research program with Kelly Tseng, PhD, Associate Professor of Pathology and Lab Medicine, School of Life Sciences at the University of Nevada, Las Vegas to characterize the effects of pharmaceutical-grade RBS on vertebrate tissue regeneration and repair.
- ◆ 2. August. Patent application *Halogenated Xanthenes as Immune Adjuvants* (17/488,430) published on the U.S. Patent and Trademark Office's (USPTO's) website.
- ◆ 3. August. Patent application Combination of Local and Systemic Therapies for Enhanced Treatment of Dermatologic Conditions (17/466,600) published on the USPTO's website.
- **4. August.** Expanded the sponsored research program with Aru Narendran, MD, PhD, Professor, Departments of Pediatrics, Oncology, Biochemistry & Molecular Biology, and Physiology & Pharmacology at the Cumming School of Medicine of the University of Calgary to investigate systemic administration of pharmaceutical-grade RBS for the treatment of pediatric leukemia.
- **3. August.** Expanded the sponsored research program with Michio Kurosu, PhD, Professor, Department of Pharmaceutical Sciences, College of Pharmacy of the University of Tennessee Health Science Center to investigate pharmaceutical-grade RBS for the treatment of anti-fungal and anti-oral bacterial infections.
- ▲ ◆ 4. September. Entered into an option agreement with the University of Miami (UM) for an exclusive worldwide license of intellectual property developed by the Ophthalmic Biophysics Center (OBC) of Bascom Palmer Eye Institute, which is part of the UM Health System, for the use of OBC's photodynamic antimicrobial therapy (PDAT) medical device in combination with pharmaceutical-grade rose bengal for the treatment of bacterial, fungal, and viral infections of the eye.
 - 5. September. Initiated a sponsored research program with OBC (UM) to investigate pharmaceutical-grade RBS for the treatment of infectious keratitis.

^{*} Since the 2022 Annual Stockholder Meeting.



2022-2023 Presentations, Publications, Patents, and Other Company Achievements

- ▲ **September 2022.** Initiated a new sponsored research program with Amina El Ayadi, PhD, Assistant Professor, Surgical Sciences Division and Jayson Jay, PhD, Postdoctoral Research Fellow and Jeane B. Kempner Scholar of the Burn, Trauma, and Critical Care Research Laboratory in the Department of Surgery at the University of Texas Medical Branch at Galveston to characterize the effects of pharmaceutical-grade RBS on full-thickness cutaneous wounds and during the subsequent phases of wound healing.
- 7. October. Expanded the sponsored research program with James G. Krueger, MD, PhD, Co-director, Center for Clinical and Translational Science, D. Martin Carter Professor in Clinical Investigation, Senior Attending Physician, and head of the Laboratory of Investigative Dermatology at The Rockefeller University to investigate the potential for PH-10 to directly alter the growth and differentiation of human keratinocytes, and to block cytokine-mediated signaling that creates different inflammatory skin diseases and may also be important in skin neoplasms.
- ♠ ◆ 8. November. The International Nonproprietary Names (INN) Expert Committee of the World Health Organization (WHO) selected RBS for the nonproprietary name of Provectus's API. The RBS name was selected by the WHO Expert Advisory Panel on the International Pharmacopoeia and Pharmaceutical Preparations, reached the status of recommended INN after a period of public consultation, and was included in INN Recommended List 88 published with the No. 3 issue of the WHO Drug Information, Volume 36.
 - **9. December.** New data from the Company's ongoing, multi-cohort, Phase 1b/2 study of the combination of PV-10 and anti-PD-1 therapy Keytruda (pembrolizumab) for the treatment of immune checkpoint blockade-naïve Stage III cutaneous melanoma were presented as a poster presentation and an oral video communication at Melanoma Bridge 2022: Response for combination of PV-10 autolytic immunotherapy and immune checkpoint blockade in stage III cutaneous melanoma



2022-2023 Presentations, Publications, Patents, and Other Company Achievements

- ◆ 10. 3Q22. Completed work with a U.S. contract development and manufacturing organization to rigorously and methodically assess lots of commercial-grade rose bengal from different specialty chemical suppliers, and compare and contrast these non-pharmaceutical grade materials with pharmaceutical-grade RBS. The preliminary results of these analyses indicate that lots of commercial-grade rose bengal had rose bengal purity that was drastically different from what was represented on their respective certificates of analysis (CofAs), and that certain lots contained gross contaminants not represented on their CofAs.
- **11. January 2023.** Preclinical research on pharmaceutical-grade RBS against colistin-resistant gram-negative bacteria was published in The Journal of Antibiotics, a medical periodical by Nature Portfolio for the Japan Antibiotics Research Association.
- **12. June.** Initiated a new sponsored research program with Nora Springer, DVM, PhD, Assistant Professor of Clinical Pathology, College of Veterinary Medicine at the University of Tennessee to evaluate the safety and preliminary efficacy of pharmaceutical-grade RBS for the ablation of canine soft tissue sarcomas.

Category	Amount	
Intellectual property	5	
Clinical development	3	
Preclinical research	7	
▲ Corporate development	1	
Drug discovery	1	Total
Manufacturing	2	19



Q&A Session

Board of Directors: Webster Bailey ● Bruce Horowitz ● Dr. Jack Lacey ● Ed Pershing ● Dominic Rodrigues



Closing Comments

Bruce Horowitz, Chief Operating Officer and Member, Board of Directors