provectus
biopharmaceuticals

Truly Transformative Cancer Immunotherapy

Small Molecule Medical Science

800 S. Gay Street, Suite 1610, Knoxville, Tennessee, USA 37929 |

Provectus is a U.S. Publicly-Traded Company: 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 Company 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," "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 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 Provectus 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.

Risks, uncertainties, and assumptions include those discussed in the Company's filings with the U.S. Securities and Exchange Commission, including those described in Item 1A of Provectus' Annual Report on Form 10-K for the period ended December 31, 2022 and the Company's Quarterly Report on Form 10-Q for the period ended September 30, 2023.

PVCT
Provectus Biopharmaceuticals, Inc.

OTCQB

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OTCQB Venture **Index**

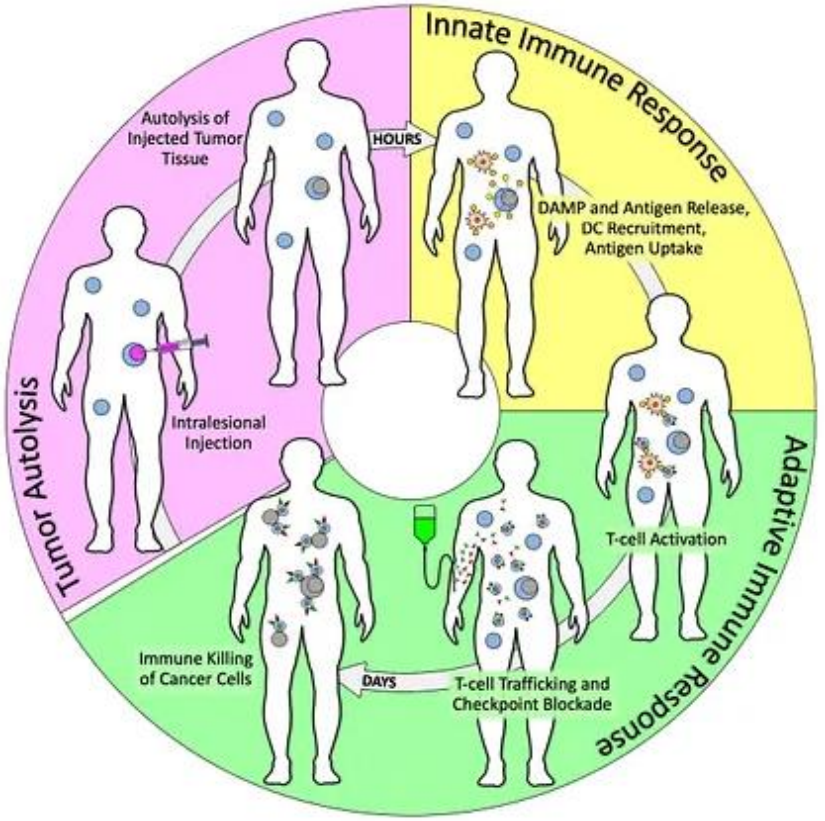
OTCMarkets Company Profile

Provectus Substack

Please note the active hyperlinks in the presentation

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

- Cancer immunotherapy agnostic to tumor type
- Small molecule drug product candidate injected into tumors on/inside the body
- 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
- ~500 patients[1]: 15+ multi-country, early-to-late-stage trials, distinct patient cohorts, expanded access programs, QoL studies: melanoma, NMSCs, HCC, liver metastases (colorectal, uveal, pancreatic, others), breast cancer
  - 25+ journal publications; 50+ medical conference presentations[2]
- Skin, liver, and breast cancers represent ~20% of 2023 estimated U.S. incidences of solid tumor disease



* DAMP = damage-associated molecular pattern. QoL = quality of life. NMSC = non-melanoma skin cancer. HCC = hepatocellular carcinoma. RIGHT IMAGE: Maintains the involvement of immune checkpoint blockade (i.e., green-colored intravenous bag) for medical combination and business rationales. [1] A total of ~2,200 superficial and hepatic malignancies injected with PV-10; A total of >900 PV-10-treatment cycles given. [2] AACR, ASCO, CIO, ECC, ENETS, ESMO, ESMO GI, ESMO IO, ISOO, Melanoma Bridge, SIR, SITC, SMR, SSO, etc.

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

Single-Agent Treatment Cutaneous/Subcutaneous Tumors	Single-Agent Treatment Visceral Hepatic Tumors	Combination Therapy Cutaneous/Subcutaneous & Visceral Hepatic Tumors
Phase 1 Metastatic Melanoma	Phase 1 Cancers of the Liver	Phase 1b/2 Cutaneous Melanoma
	• HCC; Colorectal cancer (mCRC) • Pancreatic cancer • Uveal melanoma (mUM) • Other tumor types (4+)	+Keytruda® (Phase 1b) +radiotherapy (Phase 2) • Checkpoint-naïve Stage IV • Checkpoint-refractory Stage IV • Checkpoint-naïve Stage III
Phase 2 Metastatic Melanoma		
Phase 3 RCT Locally Advanced Cutaneous Melanoma[1]	Phase 1 Metastatic Neuroendocrine Tumors	Phase 1 Metastatic Uveal Melanoma
		+Keytruda +Yervoy®+Opdivo®
Phase 1 Breast Cancer		
Intermediate-Size Expanded Access: Cu/Subcu Tumors		Single-patient Expanded Access: Cu/Subcu Tumors
• Australia (publications: 3 sites) • USA		• Multiple settings, USA +Keytruda +Opdivo +Bavencio®
QoL Study Locally Advanced Cutaneous Melanoma		

Provectus's Small Molecule Medical Science

- **Old:** Provectus proprietarily modernized a 150-year-old molecule and patented RBS's simple construction and synthesis
- **Strange:** RBS can mount the right, precise, personalized, and potentially permanent immune response to potentially cure and prevent cancer
- **Peasant:** No celebrity scientists here; global contributions from researchers, principal investigators, and academic medical centers
- **Cheap:** Everyone deserves access to leading treatments; RBS is inexpensive to manufacture
- **Odd:** Inject PV-10 into cancer directly; educate and train the immune system to finish the job and enable overwatch

* Cu/Subcu = cutaneous/subcutaneous. RCT = randomized controlled trial. mCRC = metastatic colorectal cancer. mUM = metastatic uveal melanoma. EP = endpoint. SOC = standard of care. [1] Terminated.

Single-Agent Treatment: Cutaneous/Subcutaneous & Visceral Hepatic Tumors

Cancer Indication	PV-10-Injected Disease			Overall Patient Disease					PV-10-Induced T Cell Response	CT.gov NCT
	# of Lesions (PV-10 injections cycles per lesion)	Response	Response Criteria	# of Patients	Response	Median Durability of Response	Median Survival	Response Criteria		
Meta-analysis: In-transit melanoma[1]	774 (median 1)	56% CR 64% ORR 78% DCR	mRECIST/RECIST	184	Not reported	TTR: 2.4 months TTP: Not reached TTF: Not reached	OS: 44.9 months 10-year OS: 21% DSS: 53.8 months	n/a	Yes	NCT00521053 NCT01260779 NCT02288897
Phase 1: Hepatocellular carcinoma[2]	10 (1)	30% ORR 90% DCR	mRECIST	7	Not reported	Not reported	OS: Not reached (0-112+ months) DSS: Not reached	n/a	Not measured	NCT00986661
Phase 1: Colorectal cancer metastatic to the liver[2]	6 (1)	67% DCR	mRECIST	6	Not reported	Not reported	OS: 26.8 months (0-97+ months) DSS: 26.8 months	n/a	Not measured	NCT00986661
Phase 1: Pancreatic cancer metastatic to the liver[3]	1 (1)	Not reported	n/a	1	Not reported	Not reported	OS: 29 months	n/a	Not measured	NCT00986661
Phase 1: Neuroendocrine cancer metastatic to the liver[4]	19 (median 1)	42% ORR	RECIST	12	83% DCR	PFS: 9.4 months (1.0-41.8 months)	OS: 22.5 months (5.5-42.3 months)	RECIST	Yes	NCT02693067
Phase 1: Breast cancer[5]	14 (1)	64% DCR	RECIST	12	Not reported	Not reported	Not reported	n/a	Not measured	NCT00237354

* CR = complete response. ORR = objective response rate. DCR = disease control rate. RECIST = Response Evaluation Criteria in Solid Tumors. mRECIST = modified RECIST. TTR = Time-to-response. TTP = Time-to-progression. TTF = Time-to-treatment failure. PFS = progression-free survival. OS = overall survival. DSS = disease specific survival. [1] Wachter et al. Lesion-Level Response to Single-Agent PV-10 in Stage III Cutaneous Melanoma. Society for Melanoma Research (SMR) 2021 Congress. Phase 1-3 clinical trials and expanded access programs. [2] Patel et al. Oncolytic immunotherapy of hepatic tumors with intralesional rose bengal disodium. ePoster Gallery of the canceled Society of Interventional Radiology (SIR) 2020 Annual Scientific Meeting. [3] Not presented/published. 2015-2018 Provectus care report form. [4] Price et al. Phase 1 study of Intralesional (IL) rose bengal (PV-10), an investigational autolytic immunotherapy. 2022 European Neuroendocrine Tumor Society (ENETS) Annual Conference. [5] Not presented/published. 2010 Provectus clinical study report.

Combination Therapy: Cutaneous/Subcutaneous & Visceral Hepatic Tumors

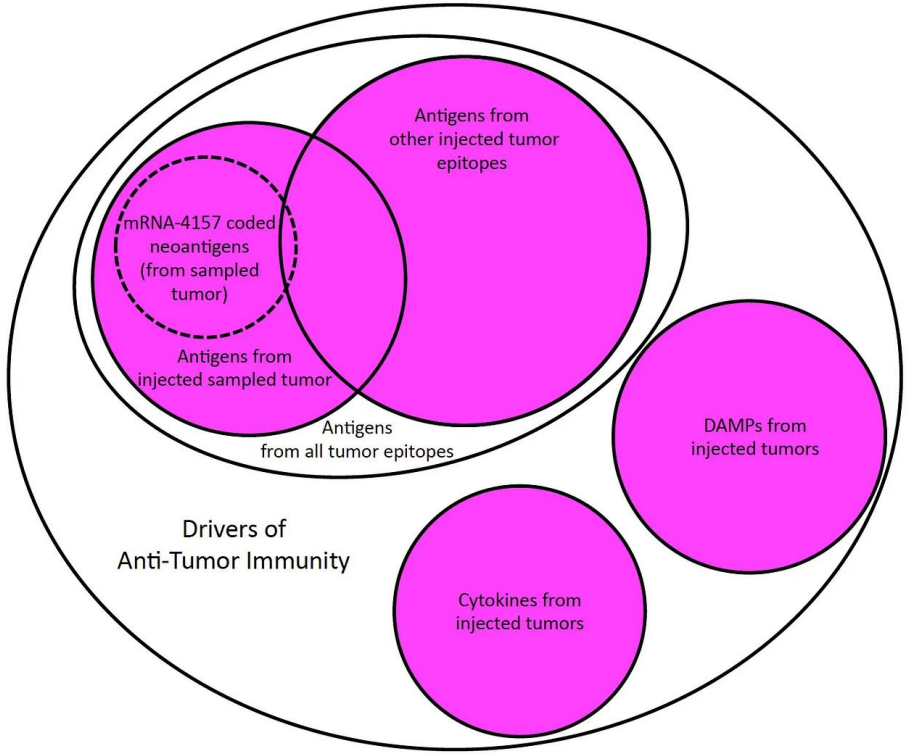
Cancer Indication (CT.gov NCT)	Combination Therapy	PV-10-Injected Disease			Overall Patient Disease					PV-10-Induced T Cell Response
		# of Lesions (PV-10 injection cycles per lesion)	Response	Response Criteria	# of Patients	Response	Median Durability of Response	Median Survival	Response Criteria	
Phase 1b: Checkpoint-naïve advanced cutaneous melanoma[1] (NCT02557321)	PV-10+PD-1	28 (median 4)	75% CR 79% ORR 86% DCR	RECIST	21	10% CR 67% ORR	PFS: 11.7 months	OS: Not reached 62% 2-year rate 5-year rate pending	RECIST	Yes
Phase 1b: Checkpoint-refractory advanced cutaneous melanoma[2] (NCT02557321)	PV-10+PD-1	Not reported	Not reported	RECIST	19	5% CR 21% ORR 53% DCR	PFS: 4.9 months	OS: 34.1 months	RECIST	Yes
Phase 1b: Stage III checkpoint-naïve melanoma[3] (NCT02557321)	PV-10+PD-1	Not reported	Not reported	RECIST	6	50% CR 83% ORR	PFS: Not reached	OS: 36.3 months (ongoing)	RECIST	Yes
Phase 1: Checkpoint-naïve/refractory uveal melanoma metastatic to the liver[4] (NCT00986661)	PV-10+PD-1, PV-10+CTLA-4+PD-1	59[a] (median 2)	19% ORR 85% DCR 7% CR 34% ORR 83% DCR	RECIST 2D-EASL	25[b]	M1a pts w/ PET-CT: 29% mCR, (mono PV-10, combo PV-10+IN)	Not reported	OS: All pts, 11 months OS: M1a, 30.6 months; M1a IN, 50.0 months OS: M1a mCRs, not reached; 100% OS rate	RECIST 2D-EASL PERCIST	Yes
Phase 2: In-transit melanoma[5] (investigator-initiated)	PV-10+ Radiotherapy	103	64% CR 85% ORR 91% DCR	RECIST	15	33% CR 87% ORR 93% DCR	Not reported	MSS: 30.6 months	RECIST	Not measured

* 2D-EASL = 2-dimensional (2D) European Association for the Study of the Liver (EASL) criteria. NED = no evidence of disease. mCR = metabolic CR. pts = patients. IN = ipilimumab+nivolumab. MSS = melanoma-specific survival. [1] Agarwala et al. A phase 1b study of rose bengal disodium and anti-PD-1 in metastatic cutaneous melanoma: results in patients naïve to immune checkpoint blockade. ESMO 2020. PV-10+pembro. [2] Zager et al. PV-10 and anti-PD-1 in cutaneous melanoma refractory to checkpoint blockade. SMR 2021. PV-10+pembro. [3] Provectus update, 2023. [4a,b] McVay et al. Metabolic complete responses in metastatic uveal melanoma patients treated with image-guided injection of PV-10. American Society of Clinical Oncology (ASCO) 2022 Annual Meeting. [b]Provectus update, 2023. PV-10, +pembro, +ipi+nivo (IN). [5] Foote et al. Results of a phase II, open-label, non-comparative study of intralesional PV-10 followed by radiotherapy for the treatment of

Part One Knowledge (*illustrative*)

- RBS is a small molecule immuno-catalyst
- PV-10 is a cancer immunotherapy potentially 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)
- 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
- Synergy and orthogonality (mechanism; activity; safety) with SOC medicines

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 the Phase Two clinical development program's 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*.

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 1a-b; 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)

Contentions: PV-10 is a cancer immunotherapy; 2nd-line PV-10 combination therapy can beat both 1st- and 2nd-line SOC mOSs

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

- Phase 1 (dedicated patient cohort); 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)

Contentions: PV-10 combination therapy mOS for M1a patients > SOC mOS; a high rate of PV-10 combination therapy mCR

3) 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

Contention: PV-10 combination therapy CR > single-agent SOC checkpoint ORR

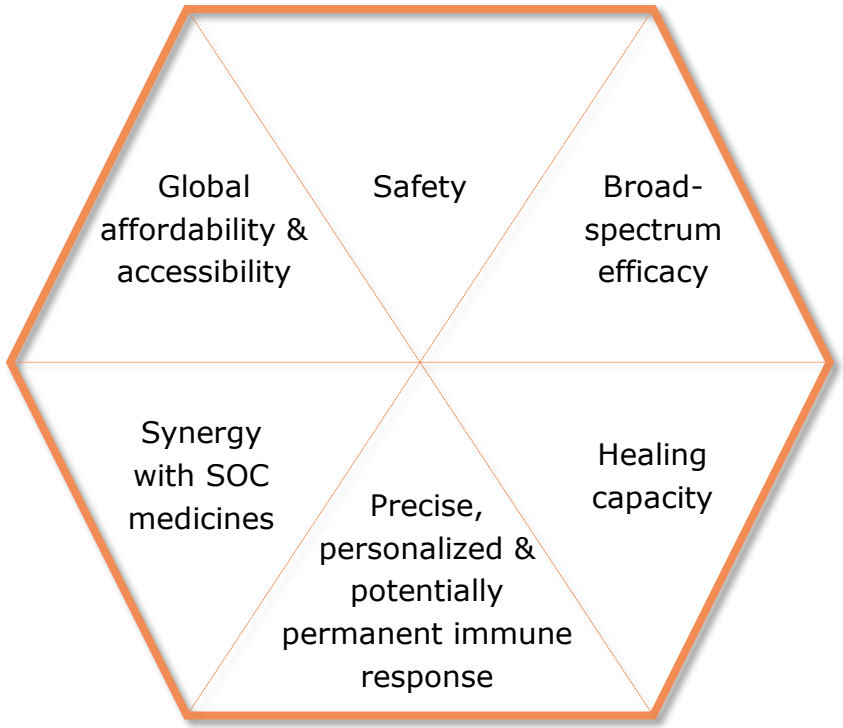
Clinical strategy: Leverage PV-10's immunotherapeutic traits and effect size to assess clinical benefit (e.g., response, durability, survival, etc.) by comparing PV-10-led treatments and actual/historical SOCs in all Part Two studies

* 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

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

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

- 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 RCT[1]
- 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)

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

VERIPURE

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).

Our Opportunity

We are building Provectus as a new kind of commercial pharma company:

⇢ Pursue cures, not treatments.

⇢ Live global health equity authentically every day.