

### **The Opportunity**

Photodynamic therapy (PDT) is an emerging modality for the treatment of neoplastic and non-neoplastic diseases.

Roswell Park Cancer Institute, a pioneer in both research and clinical applications for PDT in cancer therapy, is offering its extensive PDT patent portfolio for licensing.

### **Benefits**

The primary benefit is significantly reduced cutaneous phototoxicity enabled by the improved photosensitizing agent, HPPH, a hexyl ether derivative of pyropheophorbide-a. HPPH clears cutaneous phototoxicity in 48 hours and has enhanced tumor-killing activity on exposure to light.

A number of Phase 1 and Phase 2 clinical studies have been completed or are in progress.

HPPH offers *significantly* improved light absorption and tissue clearance vs. PHOTOFRIN and other alternatives.

### **Technology Overview**

Certain photosensitizers can be somewhat preferentially localized in cancerous tissue and, at the appropriate wavelength of light, be photoactivated to generate free radicals and singlet oxygen species that are toxic to cells and tissues.

PDT is already FDA approved for a variety of solid tumors including obstructive esophageal cancer, early- and late-stage lung cancer, and high-grade dysplasia associated with Barrett's esophagus.

Roswell Park Cancer Institute (RPCI), founded in 1898, is the nation's first cancer research, treatment and education center. RPCI is a member of the prestigious National Comprehensive Cancer Network, an alliance of the nation's leading National Cancer Institute-designated comprehensive cancer centers. Visit RPCI's website at [www.roswellpark.org](http://www.roswellpark.org).

## Photodynamic Therapy



The Roswell portfolio covers a range of technologies including:

- Multiple photosensitizing agents;
- Tumor targeting and imaging agents;
- Imaging equipment and fiber optic systems.

In addition to applications for many types of cancers, PDT has also demonstrated promise in ophthalmic (e.g. wet age-related macular degeneration) and dermatologic treatments, such as actinic keratosis and psoriasis.

### **Intellectual Property**

The intellectual property estate is extensive. Numerous foreign filings are included, as are several patent applications that are not yet in the public domain.

Principal investigators include Dr. Ravi Pandey, Dr. Thomas Dougherty, and others.

Dozens of published journal articles and the PDT Center at Roswell Park also support the technology.

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### HPPH Photosensitizers

#	Patent	Expire	Title	Unique Features
1.	5,459,159	10/17/2012	Pyropheophorbides and Their Use in Photodynamic Therapy	Photosensitive pyropheophorbides for PDT provide improved light absorption (further into red spectrum); better tissue penetration, shorter retention period in skin, greater toxicity per dose, and ease in synthesis vs. conventional PDT photosensitizers. Includes the pyropheophorbide compounds conjugated to a ligand which is capable of binding a specific receptor such as a cellular receptor, or an antibody which is capable of binding to a particular antigen; e.g. immunoglobulin (Claims 2, 5).
2.	5,314,905	05/24/2011	Pyropheophorbides Conjugates and Their Use in Photodynamic Therapy	Photosensitive pyropheophorbides for PDT provide advantages vs. photosensitizers with respect to better light absorption (further into red spectrum); better tissue penetration, shorter retention period in skin, greater toxicity per dose, and ease in synthesis.
3.	5,198,460	03/30/2010	Pyropheophorbides and Their Use in Photodynamic Therapy	Photosensitive pyropheophorbides for PDT provide advantages vs. photosensitizers with respect to better light absorption (further into red spectrum); better tissue penetration, shorter retention period in skin, greater toxicity per dose, and ease in synthesis.
4.	5,093,349	03/03/2009	Photosensitizing Agents	Photosensitive pyropheophorbides for PDT provide advantages vs. photosensitizers with respect to better light absorption (further into red spectrum); better tissue penetration, shorter retention period in skin, greater toxicity per dose, and ease in synthesis.
5.	5,002,962	03/26/2008	Photosensitizing Agents	Photosensitive pyropheophorbides for PDT provide advantages vs. photosensitizers with respect to better light absorption (further into red spectrum); better tissue penetration, shorter retention period in skin, greater toxicity per dose, and ease in synthesis.
6.	RE 38994	02/28/2023	Pyropheophorbides conjugates and their use in photodynamic therapy (Reissue of 5,314,905)	Photosensitive pyropheophorbides for photodynamic therapy (PDT). Pyropheophorbides are advantageous vs. conventional PDT photosensitizers with respect to better light absorption (further into red spectrum); better tissue penetration, shorter retention period in skin, greater toxicity per dose, and ease in synthesis. Reissued due to omission of --CH2CH2CO2R4 in substituent of Claim 1.

### Other Porphyrin Compounds

#	Patent	Expire	Title	Unique Features
7.	6,849,607	05/09/2021	Galectin Recognized Photosensitizers for Photodynamic Therapy	Carbohydrate target-specific photosensitizers as therapeutic agents for PDT. Establishes a general synthetic route for the preparation of beta-galactoside-based long wavelength absorbing photosensitizers as galectin (Gal-1) recognizing agents. The Gal-1 inhibition binding affinity of the conjugates with the parent molecule was demonstrated by ELISA assay.
8.	6,495,585	04/10/2021	Method for Treating Hyperproliferative Tissue in a Mammal	Use of xanthenone-4-acetic acid and PDT enhances the therapeutic effect and the immune response of the mammal to the hyperproliferative tissue even after the photodynamic compound and xanthenone-4-acetic acid are no longer present in the mammal.
9.	6,624,187	06/12/2020	Long Wave Length Absorbing Bacteriochlorin Alkyl Ether Analogs	Stable photosensitizer for PDT that preferentially absorbs into hyperproliferative tissue and absorbs light efficiently at a wavelength of from about 700 to about 850 nm.
10.	6,103,751	06/22/2018	Carotene Analogs of Porphyrins, Chlorins and Bacteriochlorins as Therapeutic and Diagnostic Agents	Photodynamic compounds with reduced photosensitivity. Simple derivatives of many known PDT compounds such as carotene conjugates of porphyrins, chlorins and bacteriochlorins. Carotene conjugation does not significantly reduce the tumor uptake characteristics of the photosensitizer.

11.	5,952,366	03/08/2016	Alkyl ether Analogs of Chlorins Having an N-substituted Imide Ring	Purpurinimides with lower phototoxicity, better tissue clearance, better effectiveness and which absorb at higher wave lengths (650-750 nm) for better penetration. Useful in diagnosis and treatment of certain cancers; psoriasis and papillomatosis.
12.	5,864,035	03/08/2016	Synthesis of Isoimide of Chlorins and bacteriochlorins and Their Use for Diagnosis and Treatment of Cancer	Purpurinimides with lower phototoxicity, better tissue clearance, better effectiveness and which absorb at higher wave lengths (650-750 nm) for better penetration. Chlorin and bacteriochlorin derivatives that are more convenient to synthesize. In vivo data in patent.
13.	5,770,730	03/08/2016	Synthesis of Carbodimide Analogs of Chlorins and Bacteriochlorins and Their Use for Diagnosis and Treatment of Cancer	Purpurinimides with lower phototoxicity, better tissue clearance, better effectiveness and which absorb at higher wave lengths (650-750 nm) for better penetration. Chlorin and bacteriochlorin derivatives that are more convenient to synthesize.
14.	5,591,847	05/23/2014	Long Wavelength Absorbing Photosensitizers Related to Purpurin-18, Bacteriopurpurin-18 and related Compounds With Imide Linkages	Modifications of purpurin-18 and other bacteriochlorins by converting the methyl esters to corresponding aspartyl acid derivatives to significant increase photosensitizing efficacy. Establishes the significance of hydrophilicity and hydrophobicity in localizing a photosensitizer in tumors; recommended as one of the most important requirements in designing an effective photosensitizer.
15.	5,498,710	04/22/2014	Alkyl ether Analogues of Benzoporphyrin Derivatives	Provides a series of isomerically pure benzoporphyrin derivatives (BPD) (cis- and trans- isomers) as methyl esters having utility as fluorescent and photosensitizing compounds. Such compounds may be excited by microwaves, ultrasound, and visible or infrared radiation.
16.	5,190,966	03/02/2010	Purified Hematoporphyrin Dimers and Trimers Useful in Photodynamic Therapy	Compounds for PDT that are dimers or trimers of hematoporphyrin, linked through ether linkages and obtained in isolated form, as well as dehydrated forms of these compounds. May also possess a target specific component such as an immunoglobulin, e.g. derived from polyclonal or monoclonal antibodies and may contain whole antibodies or immunologically reactive fragments.
17.	5,173,504	12/22/2009	Bacteriochlorophyll-a Derivatives Useful in Photodynamic Therapy	Tetrahydroporphyrins, such as bacteriochlorophyll-a or -b or the corresponding bacteriochlorins, for PDT and diagnostic kits. Topically or systemically administered; specifically claims a liposome carrier.
18.	5,171,741	12/15/2009	Bacteriochlorophyll-a Derivatives Useful in Photodynamic Therapy	Tetrahydroporphyrins, such as bacteriochlorophyll-a or -b or the corresponding bacteriochlorins, for PDT and diagnostic kits. Topically or systemically administered; specifically claims a diode laser as the source of irradiation.
19.	5,015,463	05/14/2008	Method to Diagnose the Presence or Absence of Tumor Tissue	Photosensitizing drugs obtained from phlorin, chlorin, or other pyrrole-containing molecules; i.e. hematoporphyrin derivatives (HpDs). Useful in diagnosis and treatment of malignant tumors.

## Instrumentation

#	Patent	Expire	Title	Unique Features
20.	6,868,221	05/08/2022	Fiber Optic Positioner	Device and method uses a multi-legged "stand" to position and hold a fiber optic treatment device in proximity to the patient's skin.
21.	6,782,167	06/07/2022	Light Beam Splitter	Efficiently and accurately splits a light beam from a fiber optic input into eight outputs where the beam powers of the output beams are within ten and preferably within five percent of each other.
22.	6,084,717	08/03/2019	Laser Beam Splitter	Efficiently and accurately splits a laser beam input into eight or more outputs where the beam energies of the output beams are within ten and preferably within five percent of each other. In particular, the eight output laser beams are able to be formed from a single laser input. Useful for PDT; e.g. with fiber optic positioners of U.S. Patent 5,671,317.
23.	5,671,317	07/16/2016	Fiber Optic Positioner	Device and method uses a multi-legged "stand" to position and hold a fiber optic treatment device in proximity to the patient's skin.
24.	5,403,308	04/04/2012	Submersible Lens Fiberoptic Assembly for Use in PDT Treatment	The fiberoptic system has a spherical zirconia lens of high refractive index which allows treatment of areas inaccessible to "forward-looking" lenses. Allows for PDT treatment of much more surface area.

25.	5,257,970	11/02/2020	In situ Photodynamic Therapy	PDT process (method) involves separately encapsulating the components in heat-sensitive liposomes. Conventional Photofrin is the preferred photosensitizer, but others may be used. The heating of the site of the tumor is accomplished by laser, ultrasound, RF, or microwave frequency.
26.	5,219,345	06/15/2010	Backscatter Monitoring System	Improvement to optical fiber treatment devices allowing for the monitoring of the condition of the light emitting tip.
27.	5,205,291	05/12/2009	In Vivo Fluorescence Photometer	A method and apparatus for in vivo fluorometry which can be implemented in a handheld nonimaging probe where sequential tissue excitation is not feasible.
28.	5,190,536	03/02/2010	Submersible Lens fiberoptic Assembly for Use in PDT Treatment	The fiberoptic system has a spherical lens of high refractive index which allows treatment of areas inaccessible to "forward-looking" lenses. Allows for PDT treatment of much more surface area.
29.	5,111,821	05/12/2009	Fluorometric Method for Detecting Abnormal Tissue Using Dual Long-Wavelength Excitation	A method and apparatus for in vivo fluorometry that can be implemented in a handheld nonimaging probe where sequential tissue excitation is not feasible.
30.	5,074,632	12/24/2008	Fiber Optic Diffusers and Methods for Manufacture of the Same	A fiber optic diffuser having an approximately uniform scattering light output and good mechanical properties and suitable for use in a biological environment.
31.	5,062,431	11/05/2008	In Vivo Fluorescence Photometer	Use of two wavelengths of light to induce fluorescence in abnormal tissue provides easy detection of abnormal tissues.

### Medical Imaging

#	Patent	Expire	Title	Unique Features
32.	7,097,826	12/23/2019	Chlorin and bacteriochlorin-based difunctional aminophenyl DTPA and N2S2 conjugates for MR contrast media and radiopharmaceuticals	Bifunctional chelate compositions and methods of detecting tumors; e.g. with HPPH-like (pyropheophorbide) compounds as imaging agents. Chelates are "bifunctional" because they bind Gd at one end and bind the target specific vehicle at the other. 48 Claims. Related to 7,078,014 and 6,534,040.
33.	7,078,014	12/23/2019	Method for using chlorin and bacteriochlorin-based aminophenyl DTPA and N2S2 conjugates for MR contrast media and radiopharmaceuticals	Methods for imaging and preparation of complexes useful for imaging tumors. 16 Claims. Related to 7,097,826 and 6,534,040.
34.	6,534,040	12/23/2019	Chlorin and bacteriochlorin-based aminophenyl DTPA and N2S2 conjugates for MR contrast media and radiopharmaceuticals	Photosensitizer compositions to deliver conjugates of variable lipophilicity (chelated with Gd or radionuclides) to tumors; i.e. Gd-HPPH contrast agents for MRI diagnosis. 22 Claims. Related to 7,097,826 and 7,078,014. Also published as 2001/0046983 (11/29/2001).
35.	5,397,777	3/14/2012	Meso poly (4-sulfonatophenyl) Porphines as MRI Image Enhancing Agents	MRI contrast agents; Mn III compounds suitable as chelates for removing manganese from chemical systems. May be administered via parenterally (IV) or by ingestion. Less toxic than TPPS4. Related to 5,236,915.
36.	5,236,915	8/17/2010	Meso poly (4-sulfonatophenyl) Porphines as MRI Image Enhancing Agents	MRI contrast agents; Mn III compounds suitable as chelates for removing manganese from chemical systems. May be administered via parenterally (IV) or by ingestion. Less toxic than TPPS4. Related to 5,397,777.