

**EXPERT DECLARATION OF MICHAEL EHRENREICH, MD,
FOR INTER PARTES REVIEW OF U.S. PATENT NO. 11,697,028**

I. INTRODUCTION

1. I, Michael Ehrenreich, submit this declaration in support of a Petition for *Inter Partes* Review of United States Patent No. 11,697,028 (“the ’028 Patent”), owned by DUSA Pharmaceuticals, Inc., (“DUSA” or “Patent Owner”). I have been retained in this matter by Polsinelli (“Counsel”) on behalf of BIOFRONTERA INC., BIOFRONTERA BIOSCIENCE GMBH, BIOFRONTERA PHARMA GMBH, and BIOFRONTERA AG (collectively, “Biofrontera” or “Petitioner”).

2. I make this declaration based upon my personal knowledge. I am over the age of 21 and am competent to make this declaration.

3. The statements herein include my opinions and the bases for those opinions, which relate to at least the following documents of the pending *inter partes* review petition:

U.S. Patent No. 11,697,028 by Thomas Boyajian et al. entitled “Adjustable Illuminator for Photodynamic Therapy and Diagnosis” (“the ’028 Patent”)

U.S. Patent No. 6,223,071 by Scott Lundahl et al. entitled “Illuminator For Photodynamic Therapy and Diagnosis Which Produces Substantially Uniform Intensity Visible Light” (“Lundahl”)

U.S. Patent Publication No. 2005/0075703 by Eric Larsen entitled “Photodynamic Stimulation Device and Methods” (“Larsen”)

U.S. Patent No. 5,079,262 by James C. Kennedy et al. entitled “Method Of Detection and Treatment Of Malignant and Non-Malignant Lesions Utilizing 5-Aminolevulinic Acid” (“Kennedy”)

4. My materials considered for forming my opinions herein have included at least the above-referenced documents. A full list of materials considered may be found in Appendix A.

5. I understand that Petitioner retained me using Rubin Anders, and that Rubin Anders is being compensated at a rate of \$650 per hour for my time spent in preparing this declaration. Regardless of my compensation in this matter, the opinions herein are my own, and I have no stake

in the outcome of the review proceeding. My compensation does not depend in any way on the outcome of Petitioner's petition.

II. QUALIFICATIONS

6. I am qualified by education and experience to testify as an expert in the field of dermatology, including photodynamic therapy (“PDT”). Attached, as Appendix B, is a copy of my curriculum vitae detailing my experience and education. Additionally, I provide the following overview of my background as it pertains to my qualifications for providing expert testimony in this matter.

7. In 1996, I earned a M.A. in Biological Sciences from Columbia University-Graduate School of Arts and Sciences in New York, NY. In 2006, I earned my M.D. degree from Rutgers New Jersey Medical School in Newark, NJ, where I was nominated for alpha omega alpha, the medical honors society.

8. Following medical school, I completed my internship at St. Barnabas Medical Center, and my residency in dermatology at SUNY Downstate Medical Center, completing my residency in 2010.

9. In 2010, I founded my own practice, SOMA Skin & Laser. I am the medical director at Soma. Since its founding in 2010, Soma has grown from a startup practice to two offices serving over 30,000 patients. Soma maintains a CLIA-certified Mohs Surgery lab, complying with all applicable standards.

10. I have also, for several years, served as the Chief of the Division of Dermatology at Newark Beth Israel Medical Center. I have published a number of papers in the field of dermatology.

11. I am a Fellow of the American Academy of Dermatology (“FAAD”) and a diplomate of the American Board of Dermatology.

12. In my practice, I regularly treat actinic keratosis (“AK”), including with Sun Pharmaceuticals BLU-U lamp in combination with LEVULAN®. In my practice, I also use BLU-U to treat acne. I believe I have been using BLU-U and LEVULAN for approximately 17 years, but certainly before the priority date of the ‘028 Patent.

13. Before my medical training, I worked in the investment and financial industry for Sanford C. Bernstein & Co., Brean Murray & Co., and Techvest, LLC, a NASD-registered broker-dealer that I founded in 1996 and sold in 2003.

14. Based on the above education and experience, I believe that I have a detailed understanding of the state of the art during the relevant period, as well as a sound basis for opining how persons of ordinary skill in the art at that time would understand the claim terms and technical issues in this case.

15. The opinions stated in this declaration are based on my own personal knowledge and professional judgment; if called as a witness during any proceeding in this matter I am prepared to testify competently about them.

16. In forming my opinions, I have considered the materials discussed and cited herein, including the asserted patent, the prosecution histories of the patent, and prior art references discussed herein, and any other references referred to or cited in this declaration.

17. Additional details regarding my qualifications and background can be found in my CV (Appendix B).

III. PERSON OF ORDINARY SKILL IN THE ART

18. I understand that the content of a patent (including its claims) and prior art should be interpreted the way a person of ordinary skill in the art would have interpreted the material at the time of invention.

19. I understand that the '028 Patent, filed on September 12, 2022, is a continuation of Application No. 16/791,004, filed on February 14, 2020 (now U.S. Patent No. 11,446,512), which is a division of Application No. 15/292,731, filed on October 13, 2016 (now U.S. Patent No. 10,589,122), which claims priority to Provisional Application No. 62/241,902, filed on October 15, 2015. Accordingly, I understand that the "time of invention" for claims 1, 2, 4-6, 16, 17, 19, 20, and 21 of the '028 Patent is October 15, 2015. All of the prior art references my opinions are based on were published more than a year before the earliest effective filing date (October 15, 2015).

20. In addition to my testimony as an expert, I am prepared to testify as someone who actually practiced in the field from 2010 to the present, who actually possessed at least the knowledge of a person of ordinary skill in the art, or member of a team skilled in the art, in that time period and as of the earliest effective filing date, and who actually treated patients using photodynamic therapy.

21. I understand that the person of ordinary skill is a hypothetical person who is assumed to be aware of all the pertinent information that qualifies as prior art. In addition, the person of ordinary skill in the art makes inferences and takes creative steps.

22. A person of ordinary skill in the art ("POSITA") at the time of the earliest effective filing date of the '028 Patent would have been an individual or member of a multi-disciplinary team with education of (1) at least a Bachelor of Science degree in one or more fields of electrical

engineering, physics, biomedical engineering, computer engineering, chemical engineering or material science, in fields relating to optics, optoelectronics, radiometry, photometry, photodynamic diagnosis (PD), photodynamic therapy (PDT), phototherapy (PT), and related technologies; and (2) a medical degree in fields relating to the diagnosis and treatment of skin conditions and related disease states. Alternatively, a POSITA individually or members of the multi-disciplinary team would have had at least four years of experience in one or more fields of optics, optoelectronics, radiometry, photometry, photodynamic diagnosis (PD), photodynamic therapy (PDT), or phototherapy (PT), and at least four years of experience in one or more fields of medical treatment of skin conditions and related disease states. A POSITA would have easily understood the prior art references referred to herein, and would have the capability to combine the teachings and draw inferences therefrom.

IV. THE '028 PATENT AND THE CURRENT DISPUTE

23. I am aware that the '028 Patent claims priority to several earlier patent applications, the earliest of which, U.S. Provisional Application No. 62/241,902, was filed on October 15, 2015. ['028 Patent at (60)].

24. I am not aware at this time of any basis for an assertion of a priority date that would be earlier than October 15, 2015. My usage of the foregoing alleged priority dates for my analyses to follow does not mean that I agree that any claims of the '028 Patent should be accorded this priority date. Even still, the references on which I base my opinions were all published well before October 15, 2015.

25. I have reviewed the '028 Patent.

26. I understand that Sun has alleged that Biofrontera has infringed the '028 Patent.

27. I understand that Biofrontera is submitting my declaration in support of a Petition for Inter Partes Review that the '028 Patent is invalid.

V. PHYSIOLOGY OF THE SKIN AND ACTINIC KERATOSES

28. The skin is comprised of two layers, the superficial epidermis and beneath that the dermis. The epidermis is in turn comprised of several layers recognized on histology. From top to bottom these are the stratum corneum, stratum lucidum, stratum granulosum, stratum spinosum, and stratum basale.

29. Actinic Keratosis (AK) is a tumor of the epidermis comprised of a proliferation of atypical keratinocytes confined to the lower levels of the epidermis, typically less than one-third of the thickness, as seen on histology. AK lesions may be subclinical and not readily apparent to visual inspection. AK presents in sun-exposed areas and is more common in people with fair skin, fair hair, sensitivity to sunlight, and/or chronic exposure to sunlight. See S. Silapunt, L. Goldberg, M. Alam, “Topical and Light-based Treatments for Actinic Keratoses,” *Seminars in Cutaneous Medicine and Surgery*, Vol 22, No 3 (September), 2003: p 162 (“Silapunt”). I cite to this article by way of background. As a clinician with years of experience treating AK, this information is within my knowledge from my medical training, my years of practice and ongoing review of clinical literature.

30. Sun damage produces genomic mutations in epidermal keratinocytes and injury-related impairment of Langerhans cell function and the cutaneous immune system. Left untreated, AK can develop into tumors, specifically squamous cell carcinoma. See *id.*

31. AK is prevalent and a common reason for visiting the dermatologist. Among the US population, mean prevalence among persons aged 65 and older is 20%, but this may be as high as 1 in 3 among populations in the southern US. It is estimated that 60% of predisposed persons aged 40 years and older have at least one AK lesion. *Id.*

32. There are a number of ways to treat AK lesions, including pharmaceutical preparations and compounds (e.g., imiquimod, diclofenac sodium, intralesional interferon, systemic retinoids). Surgical methods of treatment include cryosurgery, curettage, shave biopsy, excision, and laser surgery. Chemical destruction of AK lesions include topic 5-fluorouracil, trichloroacetic acid and salicyclic acid. *Id.* at 162-63.

33. One common method of treating AK lesions is through the use of photodynamic therapy (PDT), using a combination of topical 5-aminolevulinic acid (ALA) and a photodynamic therapy light. The combination of ALA and PDT has been known for decades and, for instance, was described in Silapunt in 2003. *Id.* at 167-68. As I describe below, I regularly use PDT in treatment of patients.

34. In PDT, topical ALA is applied to skin with AK lesions and then covered with a dressing or bandage or saran wrap for a period of time. Light is then applied to the patient's skin.

35. Within the skin, once applied ALA diffuses and accumulates in tumors and dysplastic cells. Within cells, ALA is converted into the endogenous photosensitizer protoporphyrin IX (PpIX). PpIX absorbs light in the "400-700 nm wavelength, with maximal absorption at 410, 630, and 690 nm wavelengths, but corresponding decrease in light penetration into the skin from 6 mm at 630 nm to 1.5 mm at 410 nm." Silapunt at 167. When light is applied to the cells treated with ALA, it creates an oxygen dependent cytotoxic reaction that kills the treated cells that preferentially accumulate ALA and the reactive product PpIX. PpIX is then cleared from the cells over the course of 48 hours. *Id.*

36. Practitioners also knew that light fluence was an important factor in treating AK with PDT with various coherent and non-coherent light sources having been used. *Id.*

37. PDT with ALA can be a useful treatment option for AKs and other skin conditions. Ideally, PDT can be completed in a single treatment session, and can destroy either a single AK or numerous AK lesions within a field with limited impact on any surrounding skin that is not actinically damaged. Because the treatment is completed in an office, it is not dependent on a patient's at-home compliance with, for instance, regular application of a topical cream, such as 5-FU or imiquimod.

VI. USE OF PHOTODYNAMIC THERAPY IN MY PRACTICE

38. In my practice, I regularly treat AK. AK is a very common dermatological condition and I see a patient with AK virtually every day.

39. Several times a month, on average, I treat a patient's AK lesions with PDT. Usually, I use PDT when a patient has a number of AK lesions in a given area, such as the scalp, face, hands, or arm. Presence of several AK lesions in an area usually indicates the presence of subclinical, or unseen, AK lesions proximate to the visible AK lesions. Treating an area on such a patient is called "field therapy," meaning that the treatment is conducted on an area or "field" on the patient's skin and is an effective method for treating visible and subclinical lesions. Thus, PDT is useful therapeutic modality for treating a number of lesions at once.

40. To conduct PDT in my office, I use Sun Pharmaceuticals BLU-U lamp in combination with LEVULAN®. I believe I have been using BLU-U and LEVULAN for approximately 17 years, beginning in my dermatology residency, and believe my office has owned and operated a BLU-U lamp for over ten years. In any event, I was familiar with and had used LEVULAN and BLU-U before the 2015 priority date of the '028 Patent. In my practice, I also occasionally use BLU-U to treat acne.

41. The BLU-U lamp I use in my office has a fixed U-shape and resembles the lamp described in the Lundahl patent I reviewed.

42. More often than not, I use PDT to treat AK lesions on patient's faces and scalps. For those areas of a patient's body, a fixed U-shaped design, such as that described in Lundahl and present in the BLU-U, works for treating patients. However, AK lesions suitable for PDT therapy also occur on other areas of a patient's skin, including arms, the back of hands, and the front of the neck and upper chest. Dermatologists also sometimes use PDT off-label to treat superficial basal

cell carcinoma or squamous cell carcinoma in situ, including on patients' backs and chests, where they often occur.

43. For arms, the back of hands, and the front of the neck and upper chest, my experience using the fixed BLU-U shape that I have in my office, and which is described in Lundahl, is that it makes it hard to treat hands, arms, and necks and upper chests. In my practice, we typically resort to using pillows, instrument stands, and other jury-rigged approaches to fit the arm or hand into the treatment area and make the patient comfortable. However, this is not ideal. It is sometimes awkward and uncomfortable for the patient and it can make setting and controlling the distance between the light and the treatment area difficult, especially on a convex surface such as a forearm. Hands and dorsal forearms are typically sun exposed and often have numerous AKs in susceptible individuals. Per the LEVULAN label, the treatment surface is supposed to be 2-4" from the light source.

44. Of course, as described herein, the distance from the light source affects the fluence of the light. Fluence, or the radiant energy received by a surface per unit area, is measured in J/cm^2 . Another way to think of fluence is the "dosage" of photoactivating light received in a given area of skin.

45. In dermatology, fluence of light is important in treating many skin conditions and using various light and laser equipment to treat patients. In treatment with laser light sources, I adjust the fluence of the light source, either directly when enabled by the device's interface, or in some instances by varying the time of exposure. With PDT, the BLU-U light source that I use is merely turned on and off with no ability to adjust the fluence other than through time exposure. In other words, the intensity is fixed by the design of the device and fluence can therefore only be impacted by changing the exposure duration. Fluence is equal to Intensity multiplied by Time ($F=I$

x t) My practice is to control the fluence by following the LEVULAN label for treatment duration, which is 1000 seconds.

VII. STATE OF THE ART

46. A person of ordinary skill in the art would be aware of the fundamental tenets of photodynamic therapy (PDT).

A. Kennedy

47. PDT has known and used for decades. To take one example, U.S. Patent No. 5,079,262 (“Kennedy”) titled “Method of Detection and Treatment of Malignant and Non-Malignant Lesions Utilizing 5-Aminolevulinic Acid” was filed on July 20, 1989 and granted January 7, 1992.

48. Kennedy teaches that “a method for detecting malignant and non-malignant lesions which are sensitive to protoporphyrin IX in a patient comprising administering to said patient an effective amount of a precursor of protoporphyrin IX in the biosynthetic pathway for heme so as to induce an accumulation of protoporphyrin IX in said lesions and exposing said lesions to light having a wavelength within the absorbance spectrum of said protoporphyrin IX to thereby induce fluorescence in said lesions.” (Kennedy, 3:50-58)

49. Kennedy teaches that 5-Aminolevulinic Acid (“ALA”) is a precursor of Protoporphyrin IX (PpIX), a naturally occurring photosensitizer and the immediate precursor of heme in the heme biosynthetic pathway. (4:12-15)

50. Kennedy teaches that ALA can be administered topically or orally. (4:30-32) ALA is converted to PpIX in patients, including in skin cells. (4:12-40)

51. Kennedy teaches that one of the “preferred aspects of this invention the preferred precursor of protoporphyrin IX is 5-amino-4-oxo-pentanoic acid, otherwise known as 5-

aminolevulinic acid, and a preferred wavelength of the photoactivating light is in the range 350-640 nm, more preferably a red light of about 610-630 nm. Kennedy, 4:3-8.

52. Kennedy teaches that treatment of skin lesions was possible with a combination of photosensitizing ALA and application of light.

53. Kennedy teaches a broad range of light (350-640 nm), but also points out the ability of red light (600 – 700 nm) to pass through “a slab of human tissue 1 cm thick”, with 1 to 10% of incident red light being transmitted. Kennedy, 4:60-65.

54. Kennedy contains a number of examples of treatment areas that had been treated with PDT, including shoulders, thorax, hands, and back. *See* Kennedy 6:5-15; Kennedy 40-44.

55. Example 3 in Kennedy teaches applying 20 mg ALA in a 20% concentration or 22 mg of ALA in a 10% concentration to a patient’s skin lesions and exposing the patient to photoactivating light after waiting three hours. Kennedy 6:5-37. Example 3 contains several doses of light, including 50 mWhr/cm², 17 mWhr/cm², and 26 mWhr/cm². *See id.* An engineer skilled in the art, as defined in ¶ III.22, would know how to convert the mWhr/cm² to a measure of J/cm².

56. Examples 1, 2, 3, and 4 in Kennedy all teach applying varying concentrations of ALA—10%, 17%, 20%, and 33%—to patients’ skin. *See* Kennedy at Example 1, 2, 3 and 4, 5:47-6:47. These examples also disclose varying doses of light, including 52.5 mWhr/cm², 50 mWhr/cm², 17 mWhr/cm², 26 mWhr/cm², and 37 mWhr/cm². *See id.* All of these Examples use “a 500 watt tungsten lamp, filtered to remove both infrared (heat filter) and wavelengths below 600 nm.” Kennedy, 5:54-56. All of these examples were judged by Kennedy to result in responses, including “complete response,” “no recurrence,” “partial response,” and shrinking of lesions. *See* Kennedy at Example 1, 2, 3 and 4, 5:47-6:47. Thus, reading Kennedy, I understand that applying

ALA and exposing it to photoactivating light in the range of doses disclosed in Kennedy would likely to be therapeutically effective.

B. Lundahl

57. U.S. Patent No. 6,223,071 (“Lundahl”) titled “Illuminator for Photodynamic Therapy and Diagnosis Which Produces Substantially Uniform Intensity Visible Light” was filed on May 1, 1998 and granted April 24, 2001.

58. Lundahl incorporates Kennedy by reference, noting its use of ALA as the precursor of photoactivatable agent. Lundahl, 1:38-44.

59. Lundahl is assigned to DUSA Pharmaceuticals, Inc., the maker of BLU-U and LEVULAN. Indeed, in Figures 1 and 2 contained in Lundahl, I recognize a device similar to the BLU-U light I have had in my office for over a decade.

60. As discussed in the paragraphs below, Lundahl teaches many fundamental aspects of employing a PDT light in conjunction with ALA to treat patients. Lundahl also contains in its disclosures discussions of certain issues that would motivate a person of skill in the art to make certain changes in its design.

61. Lundahl further teaches “topically applying 5-aminolevulinic acid to the contoured surface, and irradiating the contoured surface with substantially uniform intensity visible light from a plurality of light sources generally conforming to the contoured surface.” Lundahl, 3:3-7; *see also id.* at 15:29-32 (treatment of actinic keratoses with ALA and PDT).

62. As outlined in the paragraphs below, Lundahl recites a number of principles that those administering PDT to patients will recognize as important to treating patients, including (1) wavelengths of light used in PDT (Lundahl, 2:19-26; *see also id.* 15:51-54); (2) importance of uniformity of light in PDT (Lundahl, 2:14-15, 2:35-38, 4:27-33, 6:39-45); (3) the relationship between the intensity of light and distance from a source (Lundahl, 4:23-38); (4) treatment of

contoured surfaces, like patient faces, including through the use of a U-shape lamp (Lundahl, 4:29-38).

63. Lundahl teaches that “blue light having wavelengths exceeding 400 nm (nanometers) is particularly advantageous for certain diagnostic purposes and treatments, especially when ALA is the photoactivatable agent used for PD and PDT of actinic keratosis. However, visible light in other ranges of the spectrum, particularly in the green and red ranges between 400 and 700 nm, may also be used.” Lundahl 2:19-26; *see also id.* 15:51-54 (nominal wavelength of 417 nm).

64. In PDT, the uniformity of light is important to activate the ALA because the illumination source must deposit a certain amount of energy on the treatment area. Lundahl emphasizes the importance of uniform light throughout its discussion. *See* 2:14-15 (“For therapeutic reasons it is desirable to have a power output which is uniform in intensity and color.”); 2:35-38 (“Another object of the invention is to provide an illuminator for PDT that produces visible light of consistent uniformity in terms of both spectral characteristics and intensity over a diversely contoured surface.”); 4:27-29 (“Thus, in order to achieve uniform facial or scalp irradiation, variations in output irradiance with distance must be minimized.”); 6:39-42 (“Moreover, the ‘U’ shape provides the desired irradiance and irradiance uniformity for Scalp and facial irradiation, and thus ensures that the proper visible light dosage is applied to all target areas during PDT.”).

65. Lundahl also teaches the amount of energy to be deposited on the skin. Lundahl, 15:55-67 (“Since total light Dose (J/cm)=Irradiance (W/cm) x Time (Sec), the only additional parameter that needs to be controlled for delivery of the correct treatment light dose is exposure time. This is accomplished in a preferred embodiment of the present invention by the timer which controls electrical power to the ballasts and which can be set by the physician. Data has shown that

10 J/cm² delivered from a source with an irradiance density of 10 mW/cm² produces clinically acceptable results. ... A selected light dose may also be administered by additionally or alternatively varying the irradiance density.”).

66. It is a well-known fundamental law of optics that the intensity of light received by an object is inversely proportional to the square of the distance from the source (*i.e.*, $I = 1/d^2$). Lundahl recites this rule and relates it to uniformity and shape of a light-emitting device. *See* Lundahl 4:23-38 (“The inverse square law of optics states that the intensity of light from a point Source received by an object is inversely proportional to the square of the distance from the source. Because of this behavior, distance from the source is an important variable in all optical Systems. Thus, in order to achieve uniform facial or scalp irradiation, variations in output irradiance with distance must be minimized. A flat emitting surface would not deliver a uniform light dose to all contours of the face simultaneously because the non-planar facial and Scalp Surfaces could not be placed at a constant distance from the emitting surface. To ameliorate this problem, the present invention uses a U-shaped emitting surface that more closely follows the contours of the human face and scalp, and minimizes lamp to target distance variations which in turn minimizes irradiance variations at the target.”).

C. Known Reasons to Make Changes to BLU-U and/or Lundahl

67. Lundahl discloses a lamp that is a fixed U-shape. *See* Lundahl Fig. 1. However, the lamp is fixed in shape and size and based on average shapes. *See* Lundahl 6:31-35 (“The U-shape minimizes the variations in distance between the emitter and the target, providing a uniform visible light distribution to the face or scalp of the patient; the tube dimensions were chosen based on the average dimensions of the adult human head.”). Because Lundahl is based on an average, it might not be the ideal shape and size for patients with larger or smaller heads.

68. Lundahl discloses the use of fluorescent lights. But it also discloses problems associated with use of fluorescent lights. In particular, Lundahl teaches that the uniformity of the light from fluorescent tubes varies along the length of the fluorescent tube. *See* Lundahl, 6:21-22 (“Only the more uniform center portion of the tube output is used for patient treatment.”); *id.* at 9:39-41 (“The straight section of the tube between the cathode area and curved section of the “U” tubes produces slightly more output than the center portion of the curved Section.”).

69. Lundahl also teaches that the uniformity of light emitted by the fluorescent tubes is affected by heat and discloses cooling features to attempt to mitigate the uniformity problems created by the difference in phosphor coating thickness. Lundahl, 9:47-54 (“Less cooling air flows over the middle of the tubes between the Sets of reflector vents [], causing the tube wall temperature to be higher in this region. Since the output irradiance for this tube increases (to a point) with tube wall temperature, the hotter central region of the tube produces higher output irradiances than the rest of the tube and compensates for the lower emission efficiency of the central region.”).

70. Given Lundahl’s admitted issues and the treatment objective, I believe a POSITA would have been motivated to make changes to its design. For instance, a POSITA would have been motivated to make changes to Lundahl to address the fixed nature of Lundahl’s U-shape to better treat patients that have larger or smaller heads or to treat the back, hand, or thorax recited in Kennedy’s examples.

71. Lundahl incorporates Kennedy by reference and thus motivates further exploration of additional options. Lundahl, 1:39-49. For instance, as discussed above, Kennedy teaches the advantages of using red light. Kennedy, 4:3-8. Lundahl discusses blue light as a preferred embodiment. Lundahl, 15:51-54.

72. As I describe above, I have used BLU-U to treat patient's hands, arms, and necks. These areas are not curvilinear like a face or scalp and thus are not easily amenable to be treated with the BLU-U's fixed shape, which is disclosed in Lundahl. As I describe above, in my practice, I have used pillows and other jury-rigged methods to position a patient relative to the BLU-U in order to create effective treatment.

73. Thus, my own experience in treating patients also provides motivation to make modifications to Lundahl to make it a more effective and convenient device that would more effectively position the light source relative to the patient treatment area.

74. To make those modifications, a POSITA with medical treatment experience would partner with an engineer with qualifications for designing medical treatment lamps, such as the POSITA engineer described in ¶ 22.

VIII. CLAIMS OF THE '028 PATENT

'028 Patent: Claim 5

5. A method of photodynamically diagnosing or treating a patient, comprising:
 - [a] administering 5-aminolevulinic acid (ALA) to the patient;
 - [b] positioning an illuminator proximate to the patient, the illuminator comprising five panels connected by hinged structures on inner side surfaces of adjacent panels; and
 - [c] uniformly illuminating a treatment surface of the patient with light sources disposed on the five panels of the illuminator, the five panels being positioned to allow treatment within approximately four inches of the treatment surface,
 - [d] wherein each of the five panels has two first edges and two second edges shorter than the two first edges, and
 - [e] the light sources are arranged such that a higher intensity of light is emitted proximate the second edges compared to the intensity of light emitted not proximate the second edges.

Claim 5[preamble]: *“A method of photodynamically diagnosing or treating a patient, comprising.”*

75. Lundahl discloses a “method for photodynamic treatment (PDT) or diagnosis (PD) of actinic keratosis of the scalp or facial areas of a patient” and “PDT and PD of other indications (e.g., acne) and other areas of the patient (e.g., arms, legs, etc.).” Lundahl, 1:9-17. Larsen similarly discloses a method for photodynamically diagnosing or treating a patient: “[t]he present invention relates in general to electrotherapy devices and more particularly to devices and methods for photodynamic and electromagnetic stimulation of living tissue, directly and also indirectly, by stimulation of photosensitive substances introduced into or onto living tissue.” Larsen, [0001].

76. Thus, Lundahl and Larsen each disclose the preamble of claim 5.

Claim 5[a]: *“administering 5-aminolevulinic acid (ALA) to the patient;”*

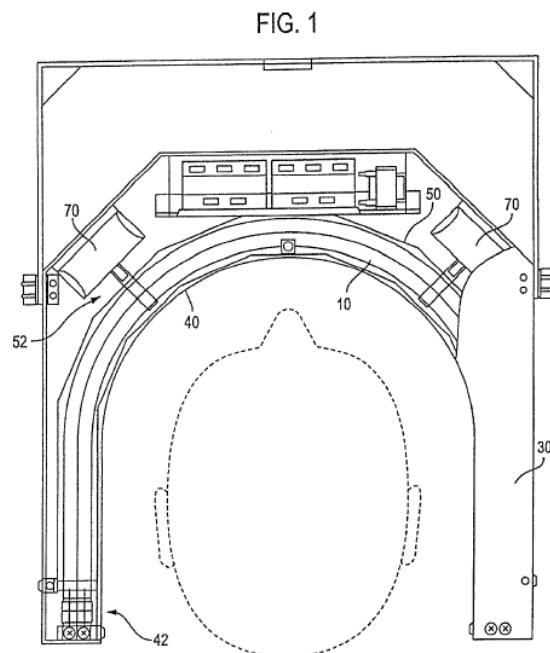
77. Lundahl teaches that “[a]ccording to one preferred embodiment of the present invention, blue light having wavelengths exceeding 400 nm (nanometers) is particularly advantageous for certain diagnostic purposes and treatments, especially when ALA is the photoactivatable agent used for PD and PDT of actinic keratosis” and that “visible light in other

ranges of the spectrum, particularly in the green and red ranges between 400 and 700 nm, may also be used.” Lundahl, 2:18-26. Lundahl describes applying ALA to a patient for the treatment of actinic keratosis, stating “One example of a treatment method for precancerous lesions, such as actinic keratosis, by PDT utilizing an illuminator described above in conjunction with 5-aminolevulinic acid (ALA) will now be described. Essentially anhydrous ALA is admixed with a liquid diluent just prior to its use. The ALA admixture is topically applied to the lesions using a point applicator to control dispersion of the ALA admixture.” *Id.*, at 15:29-37.

78. Thus, Lundahl discloses claim 5(a).

Claim 5[b]: “positioning an illuminator proximate to the patient, the illuminator comprising five panels connected by hinged structures on inner side surfaces of adjacent panels; and”

79. Lundahl teaches positioning the PDT device proximate to the patient’s head for treatment. Lundahl states “the present invention uses a U-shaped emitting surface that more closely follows the contours of the human face and scalp, and minimizes lamp to target distance variations which in turn minimizes irradiance variations at the target.” Lundahl, 4:33-38. Lundahl teaches positioning the lamp between 2 and 4 inches from the patient’s head. Lundahl 15:22-27; *see also*, Lundahl, Claim 16. Additionally, Lundahl illustrates the positioning of the PDT device proximate to the patient’s head in Fig. 1:



Id., at Fig. 1.

80. Thus, Lundahl discloses claim 5(b).

81. For the remainder of claim element 5[b], describing the illuminator, the physician defined in the POSITA definition contained in paragraph 22 would defer to a POSITA with engineering experience.

[c] uniformly illuminating a treatment surface of the patient with light sources disposed on the five panels of the illuminator, the five panels being positioned to allow treatment within approximately four inches of the treatment surface,

[d] wherein each of the five panels has two first edges and two second edges shorter than the two first edges, and

[e] the light sources are arranged such that a higher intensity of light is emitted proximate the second edges compared to the intensity of light emitted not proximate the second edges.

82. For claim elements of Claim 5[c]-[e] further describing the illuminator, the physician defined in the POSITA definition contained in paragraph 22 would defer to a POSITA with engineering experience.

Claim 6

Claim 6: *“The method of claim 5, wherein the illuminating comprises outputting red light during at least part of the time when the treatment surface is illuminated.”*

83. Lundahl teaches that “[a]ccording to one preferred embodiment of the present invention, blue light having wavelengths exceeding 400 nm (nanometers) is particularly advantageous for certain diagnostic purposes and treatments, especially when ALA is the photoactivatable agent used for PD and PDT of actinic keratosis” and that “visible light in other ranges of the spectrum, particularly in the green and red ranges between 400 and 700 nm, may also be used.” Lundahl, 2:18-26.

84. Kennedy teaches that red light was preferred for PDT, as it penetrates deeper into the skin, as compared to blue light, and PpIX (the compound produced by topical application of ALA) strongly absorbs red light. Kennedy states “[a] method of detecting and treating malignant and non-malignant tissue abnormalities and lesions of the skin” in which “5-aminolevulinic acid is administered to the patient.” Kennedy, Abstract. Kennedy states that “[i]n preferred aspects of this invention the preferred precursor of protoporphyrin IX is 5-amino-4-oxo-pentanoic acid, otherwise known as 5-aminolevulinic acid, and a preferred wavelength of the photoactivating light is in the range 350-640 nm, more preferably a red light of about 610-630 nm.” Kennedy, 4:3-8. Kennedy also states that “[t]he wavelength of the photoactivating light is of some importance, as it has been shown that between 1 and 10 percent of incident red light (600-700 nm) can pass through a slab of human tissue 1 cm thick, whereas only 0.001 percent or less of blue light (about 400 nm) can pass through the same thickness of human tissue. The photosensitizer will, therefore, be more successful if it strongly absorbs red light. PpIX does strongly absorb red light.” Kennedy, 4:60-68. Examples 1-4 in Kennedy also discuss the use of “a 500 watt tungsten lamp, filtered to

remove both infrared (heat filter) and wavelengths below 600 nm.” Kennedy, 5:54-56. Light above 600 nm wavelength, and excluding infrared, includes red light.

85. Larsen discloses outputting red light during at least part of the time when the treatment surface is illuminated: “devices are available for the photodynamic stimulation of human cell energy in the form of red and infrared radiation emitted by laser diodes and semiconductor diodes.” Larsen, [0024]. Larsen also teaches using light radiation within the wavelength of 300–2000 nm, which includes red light. *Id.*, [0025], [0071], [0076].

86. Thus, a POSITA would understand that Lundahl, Kennedy, and Larsen all teach the use of red light in combination with PDT for treating patients. For the remainder of the elements of Claim 5, the physician defined in the POSITA definition contained in paragraph 22 would defer to a POSITA with engineering experience.

IX. CONCLUSION

87. In my opinion, the prior art would motivate a skilled artisan treating patients to seek to collaborate with a optical engineer or designer to improve the light source to make it adjustable with respect to distance from the treatment area in multiple dimensions to achieve more uniform intensity and dosing for areas not well accommodated by a fixed-U-shaped device, such as forearms, hands, neck and upper chest, as well as to better accommodate statistical outliers with regard to face/scalp/head size.

88. I reserve the right to supplement my opinions in the future to respond to any arguments raised by the owner of the '028 Patent and to take into account new information that becomes available to me.

89. I declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code.

Signed on this 19th day of August, 2024, in South Orange, New Jersey.

Respectfully submitted,

Signed by:

0C33FEF67FDF450
 Michael Ehrenreich, MD

APPENDIX A
MATERIALS CONSIDERED

All Materials Referenced in this Declaration, and other Relevant Materials, Including the Following:

- U.S. Patent No. 11,697,028
- S. Silapunt, L. Goldberg, M. Alam, *Topical and Light-based Treatments for Actinic Keratoses*, SEMINARS IN CUTANEOUS MEDICINE AND SURGERY, Vol 22, No 3 (2003)
- DUSA Pharmaceuticals, Inc, Levulan® Kerastick® Label, <https://www.fda.gov/drugsatfda> (2010)
- U.S. Patent No. 5,079,262
- U.S. Patent No. 6,223,071
- U.S. Patent Publication No. 2005/0075703
- Petition for *Inter Partes* Review of U.S. Patent No. 11,697,028

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WORK EXPERIENCE

SOMA Skin & Laser (Millburn, NJ & Paramus, NJ) 2010-Present

Medical Director /Founder

- Founded dermatology practice, now in 14th year of operation
- Grew practice from startup to two offices, 30,000+ patients
- Maintain a CLIA-certified Mohs Surgery lab, complying with all applicable standards
- Expert in laser, light and energy-based therapies, including: photodynamic therapy, V-beam, Excimer, q-switched Nd:YAG, long-pulsed ND-YAG, fractional CO2, RF, and miraDry

Techvest, LLC (New York, NY) 1996-2002

Founder

- Founded boutique NASD-registered broker-dealer
- Launched two investment conferences, one in the U.S. and one in Amsterdam, attended by 140 presenting companies and hundreds of investors
- Published investment research on public companies and raised capital in private placements
- Sold company to Rodman & Renshaw in 2003

Brean Murray & Co (New York, NY) 1994-1996

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Sanford C. Bernstein & Co. (New York, NY) 1990-1992

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EDUCATION

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B.S. Finance 1990

PUBLICATIONS

- Ehrenreich M and Ruszczak Z. Update on Dermal Substitutes. Acta Dermatovenerol Croat. 2006;14(3):172-87.
- Ehrenreich M and Ruszczak Z. Update on Tissue-Engineered Biological Dressings. Tissue Engineering. 2006 Sep;12(9):2407-24.
- Ehrenreich M and Ruszczak Z. Tissue-Engineered Temporary Wound Coverings—Important Options for the Clinician. Acta Dermatovenerol Alp Panonica Adriat. 2006 Mar;15(1):5-13.
- Ehrenreich M et al. Incontinentia Pigmenti (Bloch Sulzberger Syndrome) – A Systemic Disorder. Cutis. 2007 May;79(5):355-62.

BOARDS & PROFESSIONAL ORGANIZATIONS

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PATENTS

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7,914,030 Convertible Stroller/Cycle

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