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Patent Trial and Appeal Board
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Inter Partes Review of U.S. Patent No.8,603,506
Exhibit Cover Letter Per 37 C.F.R. § 42.6(e)(4)(ii)

Dear Patent Trial and Appeal Board:

This transmittal letter identifies Exhibits 1001-1073, being filed concurrently with the present Petition for *Inter Partes* Review. Pursuant to 37 C.F.R. § 42.6(e)(4)(ii), the Certificate of Service attached to the end of the Petition for *Inter Partes* Review filed herewith, incorporates Exhibits 1001-1073, as listed below:

Exhibit #	Reference
1001	U.S. Patent No. 8,603,506
1002	Specification of Application No. 60/281,916 filed Apr. 5, 2001
1003	Specification of Application No. 60/325,489 filed Sept. 26, 2001
1004	Declaration of Michael Payette, M.D.
1005	C.V. of Michael Payette, M.D.
1006	I. B. Sneddon, <i>A CLINICAL TRIAL OF TETRACYCLINE IN ROSACEA</i> , 78 British J. Dermatology 649-52 (Jan.-Dec. 1966)
1007	R. Marks & J. Ellis, <i>COMPARATIVE EFFECTIVENESS OF TETRACYCLINE AND AMPICILLIN IN ROSACEA A Controlled Trial</i> , II(7733) Lancet 1049-52 (Nov. 13, 1971)
1008	E.M. Saihan and J.L. Burton, <i>A double-blind trial of metronidazole versus oxytetracycline therapy for rosacea</i> , 102 British J. Dermatology 443-45 (1980)
1009	P.G. Nielsen, <i>A double-blind study of 1% metronidazole cream versus systemic oxytetracycline therapy for rosacea</i> , 109(1) British J. Dermatology 63-65 (1983)
1010	Claudio Torresani <i>et al.</i> , <i>Clarithromycin versus doxycycline in the treatment of rosacea</i> , 36(12) International J. Dermatology 942-46 (Dec. 1997)
1011	Joseph B. Bikowski, <i>Treatment of Rosacea With Doxycycline Monohydrate</i> , 66(2) Cutis 149-52 (Aug. 2000)
1012	U.S. Serial No. 13/277,789 Notice of Allowance, Oct. 9, 2013
1013	WO 2000/018230 (Ramamurthy <i>et al.</i>)

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Exhibit #	Reference
1014	E-mail from PDR Customer Service Department to Lerner, David, Littenberg, Krumholz & Mentlik Library (May 14, 2015, 13:04 EST) (on file with recipient)
1015	Beth A. Kapes, <i>Doxycycline hyclate reduces comedones by 50 percent</i> , <i>Dermatology Times</i> , 2001 Suppl. 22 (November (11)):S19
1016	U.S. Patent No. 7,211,267
1017	R. Russel Martin <i>et al.</i> , <i>Effects of Tetracycline on Leukotaxis</i> , 129(2) <i>J. Infectious Disease</i> 110-16 (Feb. 1974)
1018	Gerd Plewig, M.D. & Erwin Schöpf, M.D., <i>ANTI-INFLAMMATORY EFFECTS OF ANTIMICROBIAL AGENTS: AN IN VIVO STUDY</i> , 65(6) <i>J. Investigative Dermatology</i> 532-36 (Dec. 1975)
1019	Nancy B. Esterly <i>et al.</i> , <i>THE EFFECT OF ANTIMICROBIAL AGENTS ON LEUKOCYTE CHEMOTAXIS</i> , 70(1) <i>J. Investigative Dermatology</i> 51-55 (1978)
1020	U.S. Patent No. 7,232,572
1021	L.M. Golub <i>et al.</i> , <i>Minocycline reduces gingival collagenolytic activity during diabetes Preliminary observations and a proposed new mechanism of action</i> , 18(5) <i>J. Periodontal Research</i> 516-26 (1983)
1022	L.M. Golub <i>et al.</i> , <i>A Non-antibacterial Chemically-modified Tetracycline Inhibits Mammalian Collagenase Activity</i> , 66(8) <i>J. Dental Research</i> 1310-14 (Aug. 1987)
1023	Waldemar Pruzanski <i>et al.</i> , <i>INHIBITION OF ENZYMATIC ACTIVITY OF PHOSPHOLIPASES A2 BY MINOCYCLINE AND DOXYCYCLINE</i> , 44(6) <i>Biochemical Pharmacol.</i> 1165-70 (1992)
1024	Ashok R. Amin <i>et al.</i> , <i>A novel mechanism of action of tetracyclines: Effects on nitric oxide synthases</i> , 93(24) <i>Proc. Nat'l Acad. Sci. USA</i> . 14014-019 (Nov. 1996)
1025	Ashok R. Amin <i>et al.</i> , <i>Post-transcriptional regulation of inducible nitric oxide synthase mRNA in murine macrophages by doxycycline and chemically modified tetracyclines</i> , 410(2-3) <i>FEBS Letters</i> 259-64 (June 1997)
1026	U.S. Patent No. 7,014,858
1027	L.M. Golub <i>et al.</i> , <i>TETRACYCLINES INHIBIT CONNECTIVE TISSUE BREAKDOWN BY MULTIPLE NON-ANTIMICROBIAL MECHANISMS</i> , 12(2) <i>Advances in Dental Research</i> 12-26 (Nov. 1998)
1028	Kari K. Eklund & Timo Sorsa, <i>Tetracycline Derivative CMT-3 Inhibits Cytokine Production, Degranulation, and Proliferation in Cultured Mouse and Human Mast Cells</i> , 878 <i>Annals N.Y. Academy Sciences</i> 689-91 (1999)
1029	Keith L. Kirkwood <i>et al.</i> , <i>Non-antimicrobial and Antimicrobial Tetracyclines Inhibit IL-6 Expression in Murine Osteoblasts</i> , 878 <i>Annals N.Y. Academy Sciences</i> 667-70 (1999)

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Exhibit #	Reference
1030	Y.H. Thong & A. Ferrante, <i>Inhibition of mitogen-induced human lymphocyte proliferative responses by tetracycline analogues</i> , 35(3) Clin. exp. Immunol. 443-46 (1979)
1031	A. Naess <i>et al.</i> , <i>In vivo and in vitro effects of doxycycline on leucocyte membrane receptors</i> , 62(2) Clin. exp. Immunol. 310-14 (1985)
1032	Hirohko Akamatsu <i>et al.</i> , <i>Effect of Doxycycline on the Generation of Reactive Oxygen Species: A Possible Mechanism of Action of Acne Therapy with Doxycycline</i> , 72(3) Acta Dermo-Venereologica 178-79 (1992)
1033	Y. Ueyama <i>et al.</i> , <i>Effects of antibiotics on human polymorphonuclear leukocyte chemotaxis in vitro</i> , 32(2) British J. Oral Maxillofacial Surgery 96-99 (1994)
1034	Thomas Jansen MD & Gerd Plewig MD, <i>Rosacea: classification and treatment</i> , 90(3) J. Royal Society Med. 144-50 (Mar. 1997)
1035	R. Marks, <i>Histogenesis of the Inflammatory Component of Rosacea</i> , 66(8) Proc. roy. Soc. Med. 742-45 (Aug. 1973)
1036	U.S. Patent No. 8,052,983
1037	R.K. Curley & J.L. Verbov, <i>Stevens-Johnson syndrome due to tetracyclines — a case report (doxycycline) and review of the literature</i> . 12(2) Clinical and Experimental Dermatology 124-25 (Mar. 1987)
1038	R.M. Truëb & G. Burg, <i>Acute Generalized Exanthematous Pustulosis due to Doxycycline</i> , 186(1) Dermatology 75-78 (1993)
1039	Lori E. Shapiro <i>et al.</i> , <i>Comparative Safety of Tetracycline, Minocycline, and Doxycycline</i> , 133(10) Archives of Dermatology 1224-30 (Oct. 1997)
1040	Application Serial No. 11/876,478 Specification, filed Oct. 22, 2007
1041	Jerry D. Smilack M.D., <i>The Tetracyclines</i> , 74(7) Mayo Clinic Proc. 727-29 (July 1999)
1042	PERIOSTAT. (2000). In <i>Physicians' Desk Reference</i> 944-46 (54th ed. 2000) Montvale, NJ: PDR Network
1043	ORACEA™ (2007). In <i>Physicians' Desk Reference</i> 1000-100 (61st ed 2007), Retrieved from http://www.pdr.net
1044	A.K. Gupta & M.M Chaudhry, <i>Rosacea and its management: an overview</i> , 19(3) J. European Academy of Dermatology and Venereology 273-85 (2005)
1045	Complaint of Galderma Laboratories, Inc. in Civil Action No. 00670, filed on July 31, 2015, in the United States District Court for the District of Delaware
1046	<i>Webster's Ninth New Collegiate Dictionary</i> 852, 958 (1983), "papules" and "pustules," respectively
1047	<i>Stedman's Medical Dictionary</i> 1023, 1175 (24th ed 1982), "papules" and "pustules," respectively

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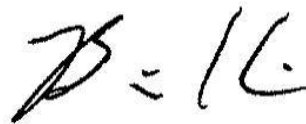
Exhibit #	Reference
1048	L.M. Golub <i>et al.</i> , <i>Low-dose doxycycline therapy: Effect on gingival and eravicular fluid collagenase activity in humans</i> , 25 J. Periodontal Research 321-30 (1990)
1049	Clay Walker <i>et al.</i> , <i>Long-Term Treatment With Subantimicrobial Dose Doxycycline Exerts No Antibacterial Effects on the Subgingival Microflora Associated With Adult Periodontitis</i> , 71(9) J. of Periodontology 1465-71 (Sept. 2000)
1050	U.S. Patent No. 4,666,897 (Golub <i>et. al.</i>)
1051	Vibramycin®.(1974). In <i>Physicians' Desk Reference</i> 942-43 (28th ed. 1974). Oradell, N.J.: PDR Network.
1052	Vital Therapies Incorporated.(2015). <i>Management</i> , Robert A. Ashely, M.A., Chief Technical Officer, Executive Vice President. Retrieved from http://vitaltherapies.com/corporate/management/
1053	Center for Drug Evaluation and Research, Fed. Food and Drug Admin., Approval Package for <u>Application Number</u> : NDA 50-744, <u>Trade Name</u> : PERIOSTAT CAPSULES, 20MG (Sept. 30, 1998), www.accessdata.fda.gov/drugsatfda_docs/nda/98/50744_appltr.pdf
1054	Mark L. Nelson & Stuart B. Levy, <i>The history of the tetracyclines</i> , 1241 Annals N.Y. Academy Sciences 17-32 (2011)
1055	Alicia Mack, <i>Examination of the Evidence for Off-Label Use of Gabapentin</i> , 9(6) J. Managed Care Pharmacy 559-68 (Nov./Dec. 2003)
1056	Thomas B. Fitzpatrick <i>et al.</i> , <i>Dermatology in General Medicine</i> (3rd ed. 1987)
1057	John Berth-Jones MRCP <i>et al.</i> , <i>The successful use of minocycline in pyoderma gangrenosum—a report of seven cases and review of the literature</i> , 1(1) J. Dermatological Treatment 23–25 (June 1989)
1058	R.K. Joshi <i>et al.</i> <i>Successful treatment of Sweet's syndrome with doxycycline</i> , 128 British J. Dermatology 584-86 (1993)
1059	P. Senet <i>et al.</i> , <i>Minocycline for the treatment of cutaneous silicone granulomas</i> , 140 British J. Dermatology 985-87 (1999)
1060	Mark Allen Berk & Allan L. Lorincz, <i>The Treatment of Bullous Pemphigoid With Tetracycline and Niacinamide. A preliminary report.</i> 122(6) Archives Dermatology 670-74 (June 1986)
1061	Carl R. Thornfeldt & Andrew W. Menkes, <i>Bullous pemphigoid controlled by tetracycline</i> , 16(2)(1) J. American Academy Dermatology 305-10 (Feb. 1987)
1062	Isabelle Thomas <i>et al.</i> , <i>Treatment of generalized bullous pemphigoid with oral tetracycline</i> , 28(1) J. American Academy Dermatology 74-77 (January 1993)
1063	David P. Fivenson <i>et al.</i> , <i>Nicotinamide and Tetracycline Therapy of Bullous Pemphigoid</i> , 130 Arch. Dermatol. 753-58 (June 1994)

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U.S. Patent and Trademark Office
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Exhibit #	Reference
1064	Ronald M. Reisner, MD, <i>Systemic Agents in the Management of Acne</i> , California Medicine 28-34 (Jan. 1967)
1065	Marsha L. Chaffins <i>et al.</i> , <i>Treatment of pemphigus and linear IgA dermatosis with nicotinamide and tetracycline: a review of 13 cases</i> , 28(6) J. Am. Acad. Dermatol. 998-1000 (June 1998)
1066	L. Reiche L <i>et al.</i> , <i>Combination therapy with nicotinamide and tetracyclines for cicatricial pemphigoid: further support for its efficacy</i> , 23(6) Clin. and Experimental Dermatol. 254-57 (Nov. 1998)
1067	Howard Maibach, MD, <i>Second-Generation Tetracyclines, A Dermatologic Overview: Clinical Uses and Pharmacology</i> , 48(5) cutis 411-17 (Nov. 1991)
1068	U.S. Serial No. 13/277,789 Fifth Preliminary Amendment, Apr. 30, 2012
1069	U.S. Serial No. 13/277,789 Official Action, May 14, 2012
1070	U.S. Serial No. 13/277,789 Resp. to May 14, 2012 Office Action, Sept. 19, 2012
1071	U.S. Serial No. 13/277,789 Resp. to November 19, 2012 Final Office Action and Substance of February 7, 2013 Interview in Reply to February 19, 2013 Interview Summary, Feb. 22, 2013
1072	U.S. Serial No. 13/277,789 Declaration under 37 C.F.R. § 1.132 [of Vasant Manna], Feb. 22, 2013
1073	MONODOX®, VIBRAMYCIN®. (2000). In <i>Physician's Desk Reference 2082-2083</i> , 2384-2386 (54th ed. 2000) Montvale, NJ: PDR Network

Respectfully submitted,

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