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**BEFORE THE PATENT TRIAL AND APPEAL BOARD**

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**WATSON LABORATORIES, INC.,**  
Petitioner,

v.

**UNITED THERAPEUTICS, INC.,**  
Patent Owner.

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Case No. IPR2017-01621  
Patent No. 9,358,240

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**PETITIONER'S REPLY IN SUPPORT OF PETITION FOR INTER  
PARTES REVIEW OF U.S. PATENT NO. 9,358,240**

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Alexandria, Virginia 22313-1450  
Submitted Electronically via the Patent Review Processing System

## PETITIONER'S EXHIBIT LIST

Exhibit	Description
1001	U.S. Patent No. 9,358,240
1002	Declaration of Maureen D. Donovan in Support of the Petition for Inter Partes Review of U.S. Patent No. 9,358,240
1003	Robert Voswinckel, et al. "Inhaled treprostinil sodium for the treatment of pulmonary hypertension" Abstract #1414, <i>Circulation</i> , 110, 17, Supplement (Oct. 2004): III-295 ("Voswinckel")
1004	U.S. Patent Application Publication No. 2004/0265238 A1 to Chaudry ("Chaudry")
1005	Hossein Ardeschi Ghofrani, Robert Voswinckel, et al., "Neue Therapieoptionen in der Behandlung der pulmonalarteriellen Hypertonie," <i>Hertz</i> , 30,4 (June 2005): 296-302 ("Ghofrani")
1006	Opti-Neb-ir® Operating Instructions, Model ON-100/2 (2005)
1007	RESERVED
1008	Venta-Neb-ir® A-I-C-I Operating Instructions, Model VN-100/4
1009	Annexes to Commission Decision C(2005)3436 of 05 September 2005, <a href="http://ec.europa.eu/health/documents/community-register/2005/2005090510259/anx_10259_en.pdf">http://ec.europa.eu/health/documents/community-register/2005/2005090510259/anx_10259_en.pdf</a> (Annex III – Ventavis® Labelling and Package Leaflet)
1010	U.S. Patent No. 6,606,989 ("Brand '989")
1011	Amendment and Reply Accompanying RCE filed in 12/591,200 (Jul. 2, 2013) (with accompanying Declaration of Lewis Rubin, M.D.)
1012	WO 93/00951 to Patton
1013	Declaration of Scott Bennett, Ph.D.
1014	Affidavit of Christopher Butler, June 15, 2017
1015	Affidavit of Christopher Butler, June 16, 2017
1016	RESERVED
1017	RESERVED
1018	U.S. Patent No. 6,521,212 ("Cloutier '212")
1019	U.S. Patent No. 4,306,075 ("Aristoff '075")
1020	U.S. Patent No. 5,190,972 ("Dumble '972")
1021	European Patent Specification 0347243 B1, published January 13, 1993
1022	U.S. Patent No. 6,261,539 ("Adjei '539")
1023	European Patent Application Publication No. EP 0372777 A2 ("Purewal EP '777")
1024	U.S. Patent No. 4,895,719 ("Radhakrishnan '719")

1025	U.S. Patent No. 5,153,222 (“Tadepalli ’222”)
1026	U.S. Patent No. 6,357,671 (“Cewers ’671”)
1027	Gessler, et al., <i>Ultrasonic versus Jet Nebulization of Iloprost in Severe Pulmonary Hypertension</i> , Eur. Respiratory J., 17:14-19 (2001)
1028	Olschewski H., et al., <i>Aerosolized Prostacyclin and Iloprost in Severe Pulmonary Hypertension</i> , 1996 Ann. Intern. Med. 124(9), 820-824 (1996) (“Olschewski 199”)
1029	Olschewski, et al., <i>Pharmacodynamics and Pharmacokinetics of Inhaled Iloprost, Aerosolized by Three Different Devices, in Severe Pulmonary Hypertension</i> , Chest J., 124(4), 1294-1304 (Oct. 2003)
1030	Byron, <i>Drug Delivery Devices: Issues in Drug Development</i> , Proc. Am. Thorac. Soc., 1:321-328 (2004)
1031	U.S. Patent No. 5,544,646 (“Lloyd”)
1032	Edwards D.A. et al., <i>Recent Advances in Pulmonary Drug Delivery Using Large Porous Inhaled Particles</i> , Journal of Applied Physiology, 85(2): 379-385 (1998) (“Edwards 1998”)
1033	Badesch, et al., <i>Prostanoid Therapy for Pulmonary Arterial Hypertension</i> , J. of the Am. C. of Cardiology, 43(12):Suppl. S (2004)
1034	U.S. Patent No. 6,054,486 (“Crow ’486”)
1035	U.S. Food and Drug Administration, Drug Approval Package: Remodulin® (approved on May 21, 2002), <a href="http://www.accessdata.fda.gov/drugsatfda_docs/nda/2002/21-272_Remodulin.cfm">http://www.accessdata.fda.gov/drugsatfda_docs/nda/2002/21-272_Remodulin.cfm</a> (“Remodulin® Approval Package”)
1036	Electronic Medicines Compendium, Ventavis®, <a href="http://www.medicines.org.uk/emc/medicine/13743">http://www.medicines.org.uk/emc/medicine/13743</a>
1037	<i>European Agency Approves Ventavis for Primary Pulmonary Hypertension</i> , P&T Community (Sep. 22, 2003), <a href="https://www.ptcommunity.com/news/2003-09-22-000000/european-agency-approves-ventavis-primary-pulmonary-hypertension">https://www.ptcommunity.com/news/2003-09-22-000000/european-agency-approves-ventavis-primary-pulmonary-hypertension</a>
1038	EU Community Register of Medicinal Products, Homepage, <a href="http://ec.europa.eu/health/documents/community-register/html/index_en.htm">http://ec.europa.eu/health/documents/community-register/html/index_en.htm</a>
1039	EMA Scientific Discussion, Ventavis® (2004), <a href="http://www.ema.europa.edu/docs/en_GB/document_library/EPAR_Scientific_Discussion/human/000474/WC500048688.pdf">http://www.ema.europa.edu/docs/en_GB/document_library/EPAR_Scientific_Discussion/human/000474/WC500048688.pdf</a>
1040	Muller et al., “Use of Inhaled Iloprost in a Case of Pulmonary Hypertension during Pediatric Congenital Heart Surgery,” 99 Anesthesiology 743-747 (2003)

1041	Mueller et al., “Inhaled Iloprost in the Management of Pulmonary Hypertension in Infants Undergoing Congenital Heart Surgery,” 21 Eur. J. Anaesthesiology (suppl. 33) 2-36 (2004)
1042	Commission Decision C(2005)3436 of 05 September 2005, <a href="http://ec.europa.eu/health/documents/community-register/2005/2005090510259/dec_10259_en.pdf">http://ec.europa.eu/health/documents/community-register/2005/2005090510259/dec_10259_en.pdf</a>
1043	EU Community Register of Medicinal Products for Human Use, Ventavis, <a href="http://ec.europa.eu/health/documents/community-register/html/h255.htm#">http://ec.europa.eu/health/documents/community-register/html/h255.htm#</a>
1044	Summary of Community Decisions, Official Journal of the European Union (Oct. 28, 2005) <a href="http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=uriserv:OJ.C_.2005.268.01.0002.01.ENG&amp;toc=OJ:C:2005:268:TOC">http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=uriserv:OJ.C_.2005.268.01.0002.01.ENG&amp;toc=OJ:C:2005:268:TOC</a> (noting a modification of marketing approval for Ventavis®)
1045	Electronic Medicines Compendium, Ventavis®, <a href="http://www.medicines.org.uk/emc/history/13743#version1">http://www.medicines.org.uk/emc/history/13743#version1</a> (noting a change to section 4.2 – Posology and Method of Administration on September 22, 2005)
1046	Voswinckel, R., et al., “Inhaled treprostinil is a potent pulmonary vasodilator in severe pulmonary hypertension,” 25 European Heart Journal 22, at 218 (2004) (“Voswinckel II”)
1047	Sulica, R and Poon, M. “Medical Therapeutics for Pulmonary Arterial Hypertension From Basic Science and Clinical Trial Design to Evidence-Based Medicine.” 3(2) Expert Rev. Cardiovas. Ther. 347-360 (2005)
1048	<i>American Heart Association’s Scientific Sessions 2004 – Largest Cardiovascular Meeting Plans to ‘Jazz It Up’ in New Orleans</i> , PR Newswire (Oct. 13 2004), <a href="http://www.prnewswire.com/news-releases/american-heart-associations-scientific-sessions-2004---largest-cardiovascular-meeting-plans-to-jazz-it-up-in-new-orleans-74293197.html#">http://www.prnewswire.com/news-releases/american-heart-associations-scientific-sessions-2004---largest-cardiovascular-meeting-plans-to-jazz-it-up-in-new-orleans-74293197.html#</a>
1049	EU Community Register of Medicinal Products, Frequently Asked Questions, <a href="http://ec.europa.eu/health/documents/community-register/register_faq_2015.pdf">http://ec.europa.eu/health/documents/community-register/register_faq_2015.pdf</a>
1050	Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004, <a href="http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2004:136:0001:0033:en:PDF">http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2004:136:0001:0033:en:PDF</a>
1051	Register of Commission Documents, European Union, <a href="https://ec.europa.eu/transparency/regdoc/index.cfm?fuseaction=home">https://ec.europa.eu/transparency/regdoc/index.cfm?fuseaction=home</a>

1052	Regulation (EC) No. 1049/2001 of the European Parliament and of the Council of 30 May 2001, <a href="http://www.europarl.europa.eu/RegData/PDF/r1049_en.pdf">http://www.europarl.europa.eu/RegData/PDF/r1049_en.pdf</a>
1053	Register of the Commission Documents, European Commission, <a href="https://ec.europa.eu/transparency/regdoc/index.cfm?fuseaction=list&amp;n=10&amp;adv=0&amp;coteId=&amp;year=2005&amp;number=3436&amp;version=ALL&amp;dateFrom=&amp;dateTo=&amp;serviceId=&amp;documentType=&amp;title=&amp;titleLanguage=&amp;titleSearch=EXACT&amp;sortBy=NUMBER&amp;sortOrder=DESC">https://ec.europa.eu/transparency/regdoc/index.cfm?fuseaction=list&amp;n=10&amp;adv=0&amp;coteId=&amp;year=2005&amp;number=3436&amp;version=ALL&amp;dateFrom=&amp;dateTo=&amp;serviceId=&amp;documentType=&amp;title=&amp;titleLanguage=&amp;titleSearch=EXACT&amp;sortBy=NUMBER&amp;sortOrder=DESC</a> (search result for document search of Commission reference number '3436' for year '2005')
1054	U.S. Patent No. 5,234,953 ("Crow '953")
1055	Declaration of DeForest McDuff, Ph.D.
1056	U.S. Patent No. 9,339,507
1057	U.S. Patent No. 6,756,033
1058	Amendment and Reply filed in 12/591,200 (May 23, 2012) (with accompanying Declaration of Lewis Rubin, M.D.)
1059	Reply in 12/,591,200 (Apr. 28, 2014)
1060	William F. Ganong, Review of Medical Physiology 591-92 (17th ed. 1995)
1061	Actelion Pharmaceuticals, "Actelion Announces Full Year 2003 Financial Results" (March 2, 2004)
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1063	Actelion Pharmaceuticals, Annual Report, 2002
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1073	Actelion Pharmaceuticals, Annual Report, 2016
1074	Adcirca, FDA Label, 5/2017
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