IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY

JANSSEN PHARMACEUTICALS, INC. and JANSSEN PHARMACEUTICA NV,	)	
Plaintiffs,	)	
v.	)	C.A. No. 2:19-cv-16484 (CCC) (MF)
MYLAN LABORATORIES LIMITED	)	
Defendant.	)	

DEFENDANT MYLAN LABORATORIES LIMITED'S INITIAL INVALIDITY CONTENTIONS

Pursuant to Local Patent Rules (L. Pat. R.) 3.3 and 3.6, and the Amended Scheduling Order (ECF No. 44), Defendant Mylan Laboratories Ltd. ("Mylan") hereby submits the following invalidity contentions to Plaintiffs Janssen Pharmaceuticals, Inc. and Janssen Pharmaceutica NV (collectively, "Plaintiffs") concerning U.S. Patent No. 9,439,906 ("the '906 patent"). In their Disclosures of Asserted Claims dated November 19, 2019, Plaintiffs state that they are asserting claims 1-21 of the '906 patent.

[redacted]

a) A. Cleton, et al. Evaluation of the pharmacokinetic profile of gluteal versus deltoid intramuscular injections of paliperidone palmitate 100 mg equivalent in patients with schizophrenia. 83 Supp. 1 Clin. Pharmacol. & Therapeutics S31, PI-75 (Mar. 2008) ("Cleton 75") (MYLANPP_0130025)

Cleton 75 published in March of 2008, prior to the earliest effective filing date of the '906 patent, and lists authors distinct from the named inventors of the '906 patent. As such, Cleton 75 is prior art to the '906 patent under pre-AIA 35 U.S.C. § 102(a).[3]

Cleton 75 discloses a multiple-dose, open-label, parallel-group study of patients with schizophrenia to investigate the PK profile of 100 mg eq. paliperidone palmitate administered into the deltoid or gluteal muscle. Cleton 75 at Abstract. Patients with schizophrenia were randomized to receive four injections into either the deltoid or gluteal muscle on days 1, 8, 36, and 64. *Id*. The study found that the median C_{max} was higher in deltoid vs. gluteal muscle after the second and fourth injections. *Id*. Further, the median concentration-time profile was higher following deltoid injection. *Id*. After four injections, median AUC_{∞} was similar for both injection sites, but C_{max} and AUC for paliperidone were 30% and 20% higher respectively in deltoid vs. gluteal muscle. *Id*. Increased median predose plasma concentrations on days 8, 36, and 64 suggested subjects were not completely at steady state after 4 injections. *Id*.

[redacted]

b) A. Cleton, et al. Assessment of the dose proportionality of paliperidone palmitate 25, 50, 100 and 150 mg eq; A new long-acting injectable antipsychotic following administration in the deltoid or gluteal muscles. 83 Supp. 1 Clin. Pharmacol. & Therapeutics S31, PI-74 (Mar. 2008) ("Cleton 74")

Cleton 74 published in March of 2008, prior to the earliest effective filing date of the '906 patent, and lists authors distinct from the named inventors of the '906 patent. As such, Cleton 74 is prior art to the '906 patent under pre-AIA 35 U.S.C. § 102(a).[4]

Cleton 74 discloses a single-dose, open-label, parallel-group study in patients with schizophrenia to evaluate dose proportionality of paliperidone palmitate injections administered in either gluteal or deltoid muscle. Data from the study indicated AUC_∞ increased proportionally with increasing paliperidone palmitate doses, regardless of gluteal or deltoid injection. Overall, deltoid injection was associated with a higher Cmax and slightly earlier tmax vs gluteal injection.

c) L. Citrome, Paliperidone: quo vadis? Int J Clin Pract, April 2007, 61, 4, 653–662 ("Citrome") (MYLANPP_0130289-98)

Citrome published in April 2007, more than one year prior to the earliest effective filing date of the '906 patent. As such, Citrome is prior art to all claims of the '906 patent under pre-AIA 35 U.S.C. § 102(b).

Citrome discloses that paliperidone was approved on December 20, 2006 by the US Food and Drug Administration for the treatment of schizophrenia. Citrome at 653. Also known as 9-hydroxy-risperidone, paliperidone is the major plasma metabolite of risperidone, an antipsychotic that was launched commercially in 1994. *Id.* Risperidone is extensively used, and has received

[redacted]

regulatory approval for the treatments of schizophrenia, bipolar mania, and more recently, irritability associated with autistic disorder in children and adolescents. *Id.* Risperidone was demonstrated in a meta-analysis to be superior to first-generation antipsychotics for the treatment of schizophrenia. *Id.*

Citrome states that several formulations of paliperidone have been tested, including an oral immediate-release formulation, an oral extended-release (ER) formulation, and a depot intramuscular formulation. *Id.* at 654. Citrome lists the clinical trials of paliperidone that were registered on http://www.clinicaltrials.gov as of November 24, 2006. *Id.* at 656. Of the 22 studies registered, 18 were with patients with schizophrenia, one with schizoaffective disorder, and three in bipolar, manic or mixed episodes. Twenty Phase III studies were listed, one Phase II study and one Phase I study. Fifteen studies were using the oral extended release formulation of paliperidone, and seven were for the depot intramuscular formulation. *Id.* at 654-55. Citrone states that clinical study NCT00210548 evaluated intramuscular injections of 50, 100 or 150 mg eq paliperidone formulated as a depot preparation vs. placebo, on days 1, 8, 36 and 64 of therapy. *Id.* at Table 1. Another study, NCT00210717, evaluated intramuscular injections of 25-100 mg eq every 4 weeks versus risperidone depot 25–50 mg every 2 weeks. *Id.*; *see also id.* (NCT00101634 evaluating intramuscular doses of 25, 50 or 100 mg eq vs. placebo and NCT00147173 evaluating intramuscular doses of 50, 100 and 150 mg eq vs. placebo). Citrone states that "depot intramuscular preparation of paliperidone holds greater promise if it can be demonstrated that it can be administered less frequently than risperidone intramuscular microspheres and that there is little lag

time prior to the development of adequate blood levels, thus eliminating the need for concurrent oral administration of an antipsychotic upon the initiation of the depot." *Id.* 660.[5]

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e) ClinicalTrials.Gov, NCT00210548 (October 10, 2006 version). ("NCT 548") (MYLANPP_0130021-22)

NCT 548 published on October 10, 2006, more than one year prior to the earliest effective filing date of the '906 patent. As such, NCT 548 is prior art to all claims of the '906 patent under pre-AIA 35 U.S.C. § 102(b).

[5] Mylan incorporates by reference herein the protocols of all clinical trials disclosed in Citrome that were publicly available as of the earliest priority date of the '906 patent.

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