

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

NALOX-1 PHARMACEUTICALS, LLC,
Petitioner

v.

ADAPT PHARMA LTD.,
OPIANT PHARMACEUTICALS,

Patent Owners

IPR2019-00692
U.S. Patent No. 9,561,177

DECLARATION OF MAUREEN DONOVAN, Ph.D.

*Inter Partes Review of U.S. Patent No. 9,561,177
Declaration of Maureen Donovan, Ph.D. (Exhibit Nalox1002)*

TABLE OF CONTENTS

I.	OVERVIEW	1
II.	MY BACKGROUND AND QUALIFICATIONS	10
III.	LEGAL STANDARDS	13
	A. Person of ordinary skill in the art.....	13
	B. Claim construction	15
	C. Anticipation and obviousness.....	16
	D. Written description and priority	19
IV.	THE '177 PATENT AND ITS CLAIMS	19
	A. Background of the art pertinent to the '177 patent	21
	1. Opioid overdose	21
	2. Prior intranasal formulations of naloxone	23
	3. Development of a new intranasal naloxone formulation.....	24
	(a) Physical and chemical properties of naloxone	25
	(b) Stability of the formulation.....	28
	(c) Nasal physiology	31
	(d) Drug exposure attributes for an improved intranasal formulation of naloxone.....	32
	(e) Choice of pharmaceutical excipients to achieve the desired exposure and stability attributes.....	34
	(f) Choice of delivery device	51
	(g) The properties of the nasal spray delivered by the spray device	52
	B. Independent claims 1, 12, and 22.....	59

*Inter Partes Review of U.S. Patent No. 9,561,177
Declaration of Maureen Donovan, Ph.D. (Exhibit Nalox1002)*

C.	Dependent claims 2–11, 13–21, and 23–30	62
D.	The '177 patent lacks priority to U.S. Provisional Application No. 61/953,379.....	65
E.	Orange Book listing of the '177 patent.....	67
V.	CLAIM CONSTRUCTION	67
1.	“pre-primed”	68
2.	“wherein no more than about [x]% of the droplets have a diameter less than 10 μm ,” “wherein the median droplet size is between about [x] μm and about [y] μm ,” and “wherein approximately 90% of droplets have a diameter less than about 100 μm ”	69
VI.	PUBLIC ACCESSIBILITY OF THE PRIOR ART.....	71
A.	A Formulator POSA exercising reasonable diligence would have located Zomig Review.....	71
VII.	BASIS OF MY ANALYSIS WITH RESPECT TO OBVIOUSNESS.....	72
A.	A Formulator POSA reading Wyse in view of HPE would have had ample reason and know-how to arrive at the subject matter of claims 1–5.....	72
1.	Claim 1	73
(a)	Preamble: “A method of treating opioid overdose, the method comprising:”	74
(b)	1.1: “delivering a 25-200 μL spray of a pharmaceutical solution”	75
(c)	1.2: “from a pre-primed device into a nostril of a patient, wherein the device is adapted for nasal delivery,”	77
(d)	1.3: “and wherein the pharmaceutical solution comprises about 4 mg naloxone hydrochloride or a hydrate thereof,”	79

***Inter Partes Review of U.S. Patent No. 9,561,177
Declaration of Maureen Donovan, Ph.D. (Exhibit Nalox1002)***

(e)	1.4: “between about 0.005% and about 0.015% (w/v) of benzalkonium chloride”.....	81
(f)	1.5: “and an isotonicity agent.”	84
2.	Claim 2	85
3.	Claim 3	86
(a)	“the pharmaceutical solution further comprises between about 0.1% and about 0.5% (w/v) of a stabilizing agent”	87
(b)	“the pharmaceutical solution further comprises . . . an amount of an acid sufficient to achieve a pH between about 3.5 and about 5.5.”	88
4.	Claim 4	89
(a)	“the isotonicity agent is sodium chloride;”	90
(b)	“the stabilizing agent is disodium edetate;”	90
(c)	“and the acid is hydrochloric acid.”	90
5.	Claim 5	91
(a)	“about 4% (w/v) naloxone hydrochloride;”	91
(b)	“about 0.74% (w/v) sodium chloride;”	93
(c)	“about 0.01% (w/v) benzalkonium chloride;”	97
(d)	“and about 0.2% (w/v) disodium edetate.”	99
B.	A Formulator POSA reading Wyse in view of Djupesland and HPE would have had ample reason and know-how to arrive at the subject matter of claims 6–9.....	101
1.	Claim 6	101
2.	Claim 7	104
3.	Claim 8	106

*Inter Partes Review of U.S. Patent No. 9,561,177
Declaration of Maureen Donovan, Ph.D. (Exhibit Nalox1002)*

4.	Claim 9	108
C.	A Formulator POSA reading Wyse in view of HPE and the '291 patent would have had ample reason and know-how to arrive at the subject matter of claims 12–15, 17–27, and 29.....	112
1.	Claim 12	113
2.	Claim 13	119
3.	Claim 14	120
4.	Claim 15	120
5.	Claim 17	124
6.	Claim 18	128
7.	Claim 19	132
8.	Claim 20	137
9.	Claim 21	139
10.	Claim 22	141
	(a) “A method of treating narcotic-induced respiratory depression,”	143
	(b) “delivering a 25-200 μ L spray . . . in a manner that delivers the pharmaceutical solution in a round spray plume with an ovality ratio less than about 2.0 when measured at 3 cm,”	144
	(c) “the patient experiences a geometric mean naloxone C_{\max} not less than about 3 ng/ml, following a single spray.”	145
11.	Claim 23	146
12.	Claim 24	146
13.	Claim 25	147

Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts



Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research



With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips



Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS

Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS

Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS

Sync your system to PACER to automate legal marketing.