

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

---

IPR2019-00693  
U.S. Patent No. 9,561,177

---

**DECLARATION OF GÜNTHER HOCHHAUS, Ph.D.**

*Inter Partes Review of U.S. Patent No. 9,561,177  
Declaration of Günther Hochhaus, Ph.D. (Nalox1003)*

**TABLE OF CONTENTS**

I.	OVERVIEW .....	1
II.	MY BACKGROUND AND QUALIFICATIONS .....	6
III.	LEGAL STANDARDS .....	9
	A. Person of ordinary skill in the art.....	10
	B. Claim construction .....	12
	C. Anticipation and obviousness.....	13
	D. Written description and priority .....	15
IV.	THE '177 PATENT AND ITS CLAIMS .....	16
	A. Independent claims 1, 12, and 22.....	17
	B. Remaining dependent claims: claims 2–11, 13–21, and 23–30.....	19
	C. The '177 patent lacks priority to U.S. Provisional Application No. 61/953,379.....	22
	D. Orange Book listing of the '177 patent.....	22
V.	STATE OF THE ART .....	23
VI.	MOTIVATION TO DESIGN A NALOXONE NASAL FORMULATION HAVING HIGH BIOAVAILABILITY, WITH A REASONABLE EXPECTATION OF SUCCESS.....	26
	A. Prior art patent applications disclose concentrated solutions of naloxone administered intranasally to treat opioid overdose.....	27
	1. Wyse (U.S. Patent No. 9,192,570).....	28
	2. Wang (Chinese Patent Publication CN 1575795) .....	28
	3. Davies (PCT Patent Publication WO 00/62757) .....	29
	B. In view of the prior art, a Pharmacologist POSA would have been motivated to design a concentrated solution of naloxone in a ready-to-use nasal delivery device, with a reasonable expectation	

***Inter Partes Review of U.S. Patent No. 9,561,177  
Declaration of Günther Hochhaus, Ph.D. (Nalox1003)***

of success.....29

1. The known physical, chemical, biopharmaceutical and pharmacological properties of naloxone and prior art would have motivated a Pharmacologist POSA to use a range of 2 to 10 mg naloxone per dose, if not up to 20 mg per dose, in an intranasal solution with a reasonable expectation of success...30
2. The nasal physiology would have motivated a Pharmacologist POSA to use an intranasal solution volume of up to 100  $\mu$ L per dose with a reasonable expectation of success. ....31
3. A Pharmacologist POSA would have been motivated to design an intranasal solution of naloxone that met or exceeded the exposure levels of the approved Narcan® 2 mg injection protocol, and would have determined that approximately 4-6 mg intranasal would work, with a reasonable expectation of success.....33
4. A Pharmacologist POSA would have been motivated to design an intranasal solution of naloxone that achieved a  $T_{max}$  within about 20-30 minutes, with a reasonable expectation of success. ....38
5. A Pharmacologist POSA would have been able to choose from the routine pharmaceutical excipients disclosed in prior art naloxone formulations, to achieve high exposure levels, with a reasonable expectation of success.....39
  - (a) A Pharmacologist POSA would have expected the inclusion of sodium chloride in a naloxone intranasal formulation to achieve high exposure levels, consistent with the Wyse intranasal formulations.....40
  - (b) A Pharmacologist POSA would have expected the inclusion of hydrochloric acid in a naloxone intranasal formulation to achieve high exposure levels, consistent with the Wyse intranasal formulations.....41
  - (c) A Pharmacologist POSA would have expected the

***Inter Partes Review of U.S. Patent No. 9,561,177  
Declaration of Günther Hochhaus, Ph.D. (Nalox1003)***

inclusion of disodium EDTA in a naloxone intranasal formulation to achieve high exposure levels, consistent with the Wyse intranasal formulations.....	42
(d) A Pharmacologist POSA would have expected the inclusion of benzalkonium chloride (BAC) in a naloxone intranasal formulation to achieve high exposure levels, and may serve to slightly improve the exposure seen with the Wyse formulations.....	42
6. A Pharmacologist POSA would have been motivated to employ a single-dose device for an intranasal formulation of naloxone, with a reasonable expectation of success.....	43
VII. CLAIM CONSTRUCTION .....	44
A. “patient”.....	45
B. “wherein the patient experiences a geometric mean naloxone C <sub>max</sub> ” .....	45
C. “wherein the patient experiences a plasma naloxone concentration such that the geometric mean of area under a plasma concentration versus time curve (AUC <sub>0-∞</sub> )” .....	46
D. “bioavailable”.....	48
VIII. PUBLIC ACCESSIBILITY OF THE APRIL 12, 2012 FDA MATERIALS .....	49
IX. CLAIMS 10, 11, 16, 22 AND 28 OF THE ’177 PATENT ARE OBVIOUS IN VIEW OF THE PRIOR ART .....	51
A. Claim 28 is obvious in view of the prior art.....	51
1. The additional limitations of claim 28 are obvious over Wyse. ....	52
2. The additional limitations of claim 28 are obvious over Wang in view of the knowledge of a Pharmacologist POSA. ....	53
3. The additional limitations of claim 28 are obvious over	

*Inter Partes Review of U.S. Patent No. 9,561,177  
Declaration of Günther Hochhaus, Ph.D. (Nalox1003)*

Wermeling 2013.....	55
B. Claim 10 and the C <sub>max</sub> limitations of claim 22 are obvious over Wyse.....	56
C. The additional limitations of claim 11 are obvious over Wyse. ....	58
D. The additional limitations of claim 16 are obvious over Wyse. ....	60
X. SECONDARY CONSIDERATIONS OF NON-OBVIOUSNESS .....	62
A. No teaching away .....	63
B. No unexpected superior results .....	64
XI. CONCLUSION.....	65

# 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.