

UNITED STATES PATENT AND TRADEMARK OFFICE

---

BEFORE THE PATENT TRIAL AND APPEAL BOARD

---

NALOX-1 PHARMACEUTICALS, LLC,  
Petitioner,

v.

ADAPT PHARMA OPERATIONS LIMITED, and  
OPIANT PHARMACEUTICALS, INC.,  
Patent Owners.

---

Case IPR2019-00694  
U.S. Patent No. 9,629,965

---

**PATENT OWNERS' RESPONSE**

**TABLE OF CONTENTS**

TABLE OF CONTENTS.....i

TABLE OF AUTHORITIES ..... iii

I. The POSA Would Not Have Been Motivated To Use Any Preservative At The Claimed Amount, Much Less BZK, Or Had A Reasonable Expectation Of Success With BZK.....4

A. Wyse Teaches Away From The Use Of BZK.....5

B. HPE Also Teaches Away From The Claimed Invention. ....13

C. The Prior Art As A Whole Also Teaches Away From BZK And Preservatives Generally.....14

D. Nalox-1 Failed To Prove Motivation To Use The Claimed Amount Of Preservative.....18

II. The Claimed 4 Milligram Initial Dose Of Naloxone Was Not Obvious.....21

A. The Prior Art Encouraged A “Low and Slow” 2 Milligram Intranasal Dose And Discouraged Higher And Faster Naloxone Dosing.....25

1. 2 Milligram Intranasal Doses Were Known To Be Effective.....25

2. The Prior Art Taught Administration of Naloxone “Low and Slow.” .....26

3. Wyse Used A 2 Milligram Intranasal Dose And Taught Away From Higher Doses. ....29

4. Wyse Does Not Disclose A Range of Doses Encompassing 4 Milligrams. ....32

5. The POSA Would Have Followed Wyse’s Approach.....34

B. Nalox-1’s Argument That The POSA Would Want “Rapid Onset” Is Unsupported And Fails to Justify A 4 Milligram Dose.....36

1. Unsubstantiated Expert Testimony Cannot Support A Motivation To Modify The Prior Art.....37

2.	The POSA Would Use The Lowest Available Comparator.....	39
3.	Nalox-1’s “Simple Math” Is Based On Faulty Assumptions.....	43
III.	Nalox-1 Did Not Prove That The Claimed Device And Method of Administration Are Obvious. ....	47
IV.	Nalox-1 Fails To Show It Would Have Been Obvious To Select And Combine The Elements Of The Claimed Invention.....	48
V.	Objective Indicia Confirm Non-Obviousness Of The Challenged Claims. ....	55
A.	The Claimed Invention Has Unexpected Properties .....	55
B.	Narcan® Nasal Spray Has Been The Subject Of Significant Skepticism. ....	57
C.	Others Failed To Arrive At The Claimed Invention And Copied It.....	57
D.	Narcan® Nasal Spray Satisfied A Long-Felt But Unmet Need.....	58
E.	Narcan® Nasal Spray Is A Commercial Success. ....	60
F.	Third Parties Have Extensively Praised Narcan® Nasal Spray.....	62
VI.	CONCLUSION.....	62

**TABLE OF AUTHORITIES**

**CASES**

*ActiveVideo Networks, Inc. v. Verizon Commc'ns, Inc.*,  
694 F.3d 1312 (Fed. Cir. 2012) .....22

*Allergan, Inc. v. Sandoz Inc.*,  
796 F.3d 1293 (Fed. Cir. 2015) .....15, 52, 53, 54, 56

*Arendi S.A.R.L. v. Apple Inc.*,  
832 F.3d 1355 (Fed. Cir. 2016) .....38, 39, 40

*AstraZeneca v. Anchen*,  
2012 WL 1065458 (D.N.J. Mar. 29, 2012),  
*aff'd*, 498 F. App'x 999 (Fed. Cir. 2013) .....48

*Avanir Pharm. v. Actavis*,  
36 F. Supp. 3d 475 (D. Del. 2014),  
*aff'd*, 612 F. App'x 613 (Fed. Cir. 2015) .....41, 42

*Bayer Pharma AG v. Watson Labs, Inc.*,  
212 F. Supp. 3d 489 (D. Del. 2016).....51

*E.I. DuPont de Nemours & Co. v. Synvina C.V.*,  
904 F.3d 996 (Fed. Cir. 2018) .....3, 23, 49

*Galderma v. Tolmar*,  
737 F.3d 731 (Fed. Cir. 2013) .....49

*Genetics Inst., LLC v. Novartis*,  
655 F.3d 1291 (Fed. Cir. 2011) .....52, 53

*Henny Penny v. Frymaster*,  
938 F.3d 1324 (Fed. Cir. 2019) .....61

*Horizon Pharma Ireland Ltd. v. Actavis Labs., UT, Inc.*,  
2017 WL 2703785 (D.N.J. May 12, 2017),  
*aff'd*, 940 F.3d 680 (Fed. Cir. 2019).....51

*In re Aller*,  
220 F.2d 454 (C.C.P.A. 1955) .....49

<i>In re Applied Materials</i> , 692 F.3d 1289 (Fed. Cir. 2012) .....	49, 51, 53
<i>In re Carlson</i> , 983 F.2d 1032 (Fed. Cir. 1992) .....	25
<i>In re Cyclobenzaprine</i> , 676 F.3d 1063 (Fed. Cir. 2012) .....	58
<i>In re Fulton</i> , 391 F.3d 1195 (Fed. Cir. 2004) .....	7, 10, 31, 32
<i>In re Gurley</i> , 27 F.3d 551 (Fed. Cir. 1994) .....	10, 14
<i>Intelligent Bio-Systems, Inc. v. Illumina Cambridge Ltd.</i> , 821 F.3d 1359 (Fed. Cir. 2016) .....	20
<i>InTouch Techs. v. VGO Commc'ns</i> , 751 F.3d 1327 (Fed. Cir. 2014) .....	12, 13
<i>K/S HIMPP v. Hear-Wear Techs., LLC</i> , 751 F.3d 1362 (Fed. Cir. 2014) .....	39
<i>Knoll Pharm. Co. v. Teva Pharm. USA, Inc.</i> , 367 F.3d 1381 (Fed. Cir. 2004) .....	58
<i>KSR Int'l Co. v. Teleflex Inc.</i> , 550 U.S. 398 (2007).....	48, 53
<i>Millennium Pharms., Inc. v. Sandoz, Inc.</i> 862 F.3d 1356 (Fed. Cir. 2017) .....	55
<i>Orexo AB v. Actavis Elizabeth LLC</i> , 903 F.3d 1265 (Fed. Cir. 2018) .....	57, 58
<i>Tec Air, Inc. v. Denso Mfg. Michigan Inc.</i> , 192 F.3d 1353 (Fed. Cir. 1999) .....	8, 18
<i>Valeant Pharm. Int'l v. Mylan Pharm.</i> , 2018 WL 2023537 (D.N.J. May 1, 2018).....	51

# 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.