

UNITED STATES PATENT AND TRADEMARK OFFICE

---

BEFORE THE PATENT TRIAL AND APPEAL BOARD

---

AQUESTIVE THERAPEUTICS, INC.,  
Petitioner,

v.

NEURELIS, INC.,  
Patent Owner.

---

Case IPR2019-00450  
Patent 9,763,876

---

**PATENT OWNER PRELIMINARY RESPONSE**  
35 U.S.C. 313

## TABLE OF CONTENTS

Patent Owner Preliminary Response .....	1
I. Precise Requested Relief .....	1
II. Statement of Reasons to Deny.....	1
A. Background.....	1
1. Epilepsy and epilepsy treatment.....	1
2. The challenged patent and claims .....	2
3. Prosecution history .....	3
B. Claim Construction.....	3
C. Denial Warranted Under Section 325(d).....	5
1. Factors a-c: The Similarities and Material Differences Between the Asserted Art and the Prior Art Involved During Examination; the Cumulative Nature of the Asserted Art and the Prior Art Evaluated During Examination; and the Extent to which the Asserted Art was Evaluated During Examination .....	8
2. Factor d: The Extent of Overlap Between the Arguments Made During Examination and the Manner in which Petitioner Relies on the Prior Art or Patent Owner Distinguishes the Prior Art.....	9
3. Factor e: Whether Petitioner has Pointed Out Sufficiently How the Examiner Erred in Its Evaluation of the Asserted Prior Art.....	20
4. Factor f: The Extent to which Additional Evidence and Facts Presented in the Petition Warrant Reconsideration of the Prior Art or Arguments .....	23
III. Conclusion .....	24
Exhibit List.....	25
Type Volume Certificate.....	26

Certificate of Service .....27

## **I. PRECISE REQUESTED RELIEF**

The patent owner (“Neurelis”) requests that institution be denied because the petitioner (“Aquestive”) has failed to demonstrate a reasonable likelihood that any challenged claim is unpatentable.

## **II. STATEMENT OF REASONS TO DENY**

### **A. BACKGROUND**

#### *1. Epilepsy and epilepsy treatment*

Epilepsy is a general term for conditions with recurring seizures, involving abnormal electrical activity in the brain that causes an involuntary change in body movement or function, sensation, awareness, or behavior. A seizure may last from a few seconds to a few minutes. Epilepsy causes include head or brain injury, brain tumor, central nervous system infection, stroke, and genetics, but in most cases the etiology is unknown. EX2004, 3; EX2001.

Epilepsy actively affects over 3.4 million people in the United States (about 1.2% of the total population), ranks as the second-most burdensome neurologic disorder worldwide in terms of disability-adjusted life years, with associated stigma, psychiatric co-morbidity and high economic costs. EX2004, 3; EX2001; EX2005, 296. In the United States alone, nearly half a million children have active epilepsy. EX2001. Medications exist to help prevent seizures, but success varies and about one-third of epileptics receiving care still experience

seizures. EX2004, 3. Uncontrolled seizures may result in injury, anxiety, depression, brain damage and death, while also interfering with normal day-to-day activities, such as working, going to school, and socializing with friends and family. EX2004, 3. Better treatments are needed to control epileptic seizures, and nasal sprays could provide the best solution. EX2003. The United States Food and Drug Administration granted Neurelis, the patent owner, a Fast Track designation to develop a diazepam intranasal solution for this very purpose. EX2002.

## *2. The challenged patent and claims*

Benzodiazepine is a family of drugs that are useful for treating seizures. EX1001, 1:29-39. While other benzodiazepine formulations for treating seizures exist, they suffer from solubility problems and can be very difficult to administer to a subject during a seizure, particularly if the person administering therapy is not a health professional. EX1001, 1:53-2:20. The present inventors realized that nasal delivery would address the drug-administration problem, and the use of vitamin E-analogs and alcohols as substantial fractions of the formulation would address the solubility problem, while still providing an acceptable nasal-delivery formulation. The alkyl glycol functions as a penetration enhancer to improve bioavailability. EX1001, 16:55-56, 34:55-58. Challenged claim 1, from which all the other challenged claims depend, defines the invention as (EX1001, 63:26-34):

A method of treating a patient with a disorder which is treatable with a benzodiazepine drug, comprising:

# 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.