

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

AQUESTIVE THERAPEUTICS, INC.

Petitioner

v.

IONO PHARMA, LLC

Patent Owner

IPR2025-00874

U.S. Patent No. 11,021,437 B2

**PETITIONER'S
FIRST UPDATED EXHIBIT LIST**

<u>EXHIBIT NO.</u>	<u>EXHIBIT DESCRIPTION</u>
EX1001	U.S. Patent No. 11,021,437 B2, entitled “Pharmaceutical Formulation For Sublingual Or Buccal Delivery Of Epinephrine Or A Pro - Drug Thereof”, filed as application serial number 16/347,625 on November 9, 2017, Almoazen inventor, issued on June 1, 2021 (“the ‘437 Patent”).
EX1002	U.S. Patent No. 3,809,714, entitled “Novel Ester Of [(Methylamino)Methyl] Benzyl Alcohol”, Hussain and Truelove inventors, issued on May 7, 1974 (“the ‘714 Patent” or “Truelove 1”).
EX1003	Ashraf M and Sayeed VA, “Considerations in Developing Sublingual Tablets – An Overview,” <i>Pharmaceutical Technology</i> 38 (11) 2014 (“Asraf”).
EX1004	U.S. Patent No. 4,136,145, entitled “Medicament Carriers In The Form Of Film Having Active Substance Incorporated Therein”, Fuchs and Hilmann inventors, issued January 23, 1979 (“the ‘145 Patent” or “Fuchs”).
EX1005	The Almoazen ‘437 Patent application prosecution history file for the ‘437 Patent, serial no. 16/347,625 (“the ‘437 File History” or Almoazen File History”).

- EX1006 U.S. Patent No. 3,825,583, entitled “Ester Of 3-Hydroxy- α -[(Methylamino) Methyl]Benzyl Alcohol”, Hussain and Truelove inventors, issued on July 23, 1974 (“the ‘583 Patent” or “Truelove 2”).
- EX1007 Hussain A and Truelove JE: “Prodrug Approaches to Enhancement of Physicochemical Properties of Drugs IV: Novel Epinephrine Prodrug”, Journal of Pharmaceutical Sciences 65(EX10), 1976 (“Truelove Article” or “Truelove 4”).
- EX1008 U.S. Patent No. 3,868,461, entitled “Ester Of 3,4-Dihydroxy-Alpha (Isopropylamino) Methyl Benzyl Alcohol Composition And Anti-Asthma Use Thereof”, Hussain and Truelove inventors, issued on February 25, 1975 (“the ‘461 Patent” or “Truelove 3”).
- EX1009 *The Merck Index*, 12th Ed., 1996, p. 613.
- EX1010 Reserved.
- EX1011 USP certificate for epinephrine, dated 14 Aug 2017.
- EX1012 The prescription information for the epinephrine used in the EpiPen.
- EX1013 The Almoazen ‘437 Patent Provisional Application for Patent, serial no. 62,421,316, filed on November 13, 2016, Hassan

Almoazen (“ ‘437 Provisional Application” or “Almoazen Provisional Application”).

- EX1014 WO2018/089570 A1 (PCT/US2017/060761), entitled “Pharmaceutical Formulation For Sublingual Or Buccal Delivery Of Epinephrine”, Almoazen and Haynes, co-inventors (“ ‘437 PCT Application” or “Almoazen PCT Application”).
- EX1015 Florence AT and Attwood D, “Physicochemical Principles of Pharmacy”, Fifth edition, Eds. Pharmaceutical Press (2011) (“Florence”).
- EX1016 U.S. Patent No. 4,145,441, entitled “Sympathomimetic Amines Exhibiting Anti-Hemorrhoidal Activity”, Bodor inventor, issued March 20, 1979 (“the ‘441 Patent” or “Bodor”).
- EX1017 U.S. Patent Application Publication No. US 2007/0202163 A1, entitled “Fast-Disintegrating Epinephrine Tablets For Buccal Or Sublingual Administration”, Rawas-Qalaji, *et al.*, inventors, published on August 30, 2007 (“Rawas-Qalaji”).
- EX1018 Ettmayer *et al.*, “Lessons Learned from Marketed and Investigational Prodrugs”. Journal of Medicinal Chemistry 47(EX10), 2393-2404, 2004 (“Ettmayer”).

- EX1019 Rautio *et al.*, “Prodrugs: design and clinical applications”.
Nature Reviews Drug Discovery 7, 255-270, 2008 (“Rautio”).
- EX1020 Silverman RB., Chapter 8, “Prodrugs and drug delivery
systems” in The Organic Chemistry of Drug Design and Drug
Action. Academic Press, Inc. 1992 (“Silverman”).
- EX1021 U.S. Patent No. 11,191,737 B2, entitled “Enhanced Delivery
Epinephrine Compositions”, Schobel, *et al.* inventors, claiming
benefit of provisional application No. 62/331,996, filed on May
5, 2016 (“Schobel”).
- EX1022 Alaadin Alayoubi, Lindsay Haynes, Hemlata Patil, Baher
Daihom, Richard Helms & Hassan Almoazen (2016):
“Development of a fast dissolving film of epinephrine
hydrochloride as a potential anaphylactic treatment for
pediatrics”, Pharmaceutical Development and Technology,
Early Online: 1-5, Published online 6 January 2016 (“Almoazen
Paper”).
- EX1023 Baldessarini, *et al.*, “Hydrolysis of diester prodrugs of
apomorphine”, Biochemical Pharmacology. Vol. 26, pp. 1749-
1756. Pergamon Press. 1977 (“Baldessarini”).

- EX1024 Kristoffersson, *et al.*, “Drug latentiation of terbutaline”, Acta Pharm. Suecica 11, 427-438 (1974) (“Kristoffersson”).
- EX1025 Christrup, *et al.*, “Improvement of buccal delivery of morphine using the prodrug approach”, Int J Pharma, 154, 1997, pp. 157-165 (“Christrup”).
- EX1026-EX1028 Reserved.
- EX1029 Lieberman, *et al.*, “The diagnosis and management of anaphylaxis practice parameter: 20EX10 update”, J Allergy Clin Immunol Sept. 20EX10 126(3):477-80.e1-42 (“Lieberman”).
- EX1030 Hansen, *et al.*, “Ketobemidone prodrugs for buccal delivery”, Acta Pharm Nord, 3 (1991) 77-82 (“Hansen 1991”).
- EX1031 den Daas, et al., “Improvement of the oral bioavailability of the selective dopamine agonist N-0437 in rats: the in vitro and in vivo activity of eight ester prodrugs”, Naunyn Schmiedeberg’s Arch Pharmacol (1990) 341:186-91 (“den Daas”).
- EX1032 Hansen, *et al.*, “Ketobemidone prodrugs for buccal delivery: Prediction of the extent of saliva-catalyzed hydrolysis of various ester prodrugs under simulated in vivo condition”, Int J Pharma, 88, 1992, pp. 229-235 (“Hansen 1992”).

- EX1033 A copy of the ‘437 Patent (Exhibit EX1001) showing where material from the Almoazen Paper (Exhibit EX1022) appears in highlighting.
- EX1034 Roche, “Design of biopharmaceutical properties through prodrugs and analogs”, American Pharmaceut. Assoc., Washington, DC, 1977 (“Roche”).
- EX1035 A copy of the Almoazen Paper (Exhibit EX1022) highlighted to show where material from the Paper appears in the ‘437 Patent (Exhibit EX1001).
- EX1036 Morrison and Boyd, “Organic Chemistry”. 2nd Edition, Chapter Sections 18.1-18-4 (1970) (“Morrision and Boyd”).
- EX1037 Streitwieser, et. al, “Introduction to Organic Chemistry”, 4th Edition, excerpts (1992) (“Streitweiser”).
- EX1038 Reserved.
- EX1039 Stepensky, *et al.*, “Long-Term Stability Study of L-Adrenaline Injections: Kinetics of Sulfonation and Racemization Pathways of Drug Degradation”, J Pharm Sci 93:969–980 (2004) (“Stepensky”).

- EX1040 Huttunen, K., Raunio, H., Rautio, J., “Prodrugs—from Serendipity to Rational Design”, *Pharmacol Rev* 63:750–771 (2011) (“Rautio II”).
- EX1041 Senel & Hincal, “*Drug permeation enhancement via buccal route: possibilities and limitations*”, *J Contr Rel* 72: 133-144, 2001 (“Senel”).
- EX1042-EX1043 Reserved.
- EX1044 Kohn, et. al, “Clinical Comparison of Dipivalyl Epinephrine and Epinephrine in The Treatment Of Glaucoma”, *American Journal of Ophthalmology* 87:196-201, 1979 (“Kohn”).
- EX1045 Reserved.
- EX1046 *Journal of Medicinal Chemistry*, “Manuscript Submission Requirements Checklist”, https://researcher-resources.acs.org/publish/author_guidelines?coden=jmcmar#manuscript_submission_requirements_checklist, October 29, 2024 (“JMC Manuscript Requirements”).
- EX1047-EX1049 Reserved.
- EX1050 Declaration of Jarkko Rautio, Ph.D.
- EX1051 Declaration of Nicholas A. Meanwell, Ph.D.

- EX1052 **‘437 PCT File History** – PCT/US2017/060761, filed November 9, 2017.
- EX1053 A copy of the ‘437 Provisional Application (EX1013) highlighted to show where material from the Almoazen Paper (EX1022) appears.
- EX1054 **Schobel Provisional**, Provisional Application, serial no. 62/331,996, filed May 5, 2016, to Schobel U.S. 11,191,737.
- EX1055-1059 Reserved.
- EX1060 Motosue, *et al*, “Risk factors for severe anaphylaxis in the United States”, *Ann Allergy Asthma Immunol* 119 (2017) 356-361.
- EX1061 Dribin, et al., “Anaphylaxis definition, overview, and clinical support tool: 2024 consensus report—a GA²LEN project”, <https://doi.org/10.1016/j.jaci.2025.01.021>
- EX1062 U.S. Patent No. 12,023,309.
- EX1063 U.S. Patent No. 11,273,131.
- EX1064 Excerpts of quarterly report for the period ending 6-30-2025 filed with the SEC by Aquestive Therapeutics.
- EX1065 Aquestive 6-16-2025 Press Release.

- EX1066 Excerpts of 2023 annual report filed with the SEC by Aquestive Therapeutics.
- EX1067 Excerpts of 2024 annual report filed with the SEC by Aquestive Therapeutics.
- EX1068 Excerpts of quarterly report for the period ending 3-31-2025 filed with the SEC by Aquestive Therapeutics.
- EX1069 Excerpts of quarterly report for the period ending 6-30-2025 filed with the SEC by Aquestive Therapeutics.
- EX1070 Prescription Drug User Fee Amendments,
<https://www.fda.gov/industry/fda-user-fee-programs/prescription-drug-user-fee-amendments>.
- EX1071 5-27-2016 email from Steve Wargacki to Ramona McCudden re: Possible candidate source.
- EX1072 6-3-2016 email from Ramona McCudden to Steve Wargacki re: MonoSol Rx (2).
- EX1073 6-16-2016 email from Ramona McCudden to Steve Wargacki re: MonoSol Rx (1).
- EX1074 10-23-2016 email from Steve Wargacki to Ramona McCudden re: email from Almoazen.

EX1075 Declaration of Romona Mccudden, Recruiting Specialist at
Petitioner Aquestive Therapeutics, Inc.

Dated: September 18, 2025

Respectfully submitted,

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CERTIFICATE OF SERVICE

I hereby certify that on September 18, 2025, a complete copy of the foregoing Petitioner's First Updated Exhibit List, and all listed exhibits not already of record in this proceeding on P-TACTS, were served on counsel of record for the Patent Owner by filing this document and the exhibits through P-TACTS and by sending this document and the exhibits via electronic mail and/or links to the following addresses:

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