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

IPR2019-00691
U.S. Patent No. 9,561,177

DECLARATION OF GÜNTHER HOCHHAUS, Ph.D.

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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

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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 µL 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

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   (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

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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

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B. "wherein the patient experiences a geometric mean naloxone C_{max}" 45

C. "wherein the patient experiences a plasma naloxone concentration such that the geometric mean of area under a plasma concentration versus time curve ($AUC_{0-\infty}$)" 46

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3. The additional limitations of claim 28 are obvious over

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B. Claim 10 and the C_{max} limitations of claim 22 are obvious over Wyse. 56

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