Eptinezumab Demonstrates Early Relief from Episodic and Chronic Migraine: Consistency of Effect Across 4 Clinical Trials

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Disclosures

Relevant: *Personal fees*: Alder BioPharmaceuticals

Other: *Personal fees:* Amgen, Autonomic technologies, Axsome, Aural Analytics, Allergan, Biohaven, Charleston Laboratories, Dr Reddy's Laboratories/Promius, Electrocore LLC, Eli Lilly, eNeura, Foresite Capital, Ipsen, Impel, Neurolief, Novartis, Oppenheimer, Satsuma, Supernus, Sun Pharma (India), Theranica, Teva, Vedanta, WL Gore, Zosano, ZP Opco; *CME fees or royalty payments:* Healthlogix, Medicom, Medlogix, Mednet, Miller Medical, PeerView, WebMD/Medscape, Chameleon, Academy for Continued Healthcare Learning, Universal Meeting Management, Haymarket , Global Scientific Communications, UpToDate, Oxford University Press, Cambridge University Press, Wolters Kluwer; *Stock options:* Aural Analytics, Healint, Theranica, Second Opinon/Mobile Health, Epien, GBS/Nocira, Matterhorn/Ontologics, King-Devick Technologies; *Consulting without fee:* Aural Analytics, Healint, Second Opinion/Mobile Health, Epien; *Board of Directors:* Epien, Matterhorn/Ontologics, King-Devick Technologies; *Patent:* 17189376.1-1466:vTitle: Botulinum Toxin Dosage Regimen for Chronic Migraine Prophylaxis without fee; *Professional society fees or reimbursement for travel:* American Academy of Neurology, American Brain Foundation, American Headache Society, American Migraine Foundation, International Headache Society, Canadian Headache Society; *Other: Use agreement through employer:* Myndshft

Early and robust onset of effect is important for optimal preventive migraine treatment

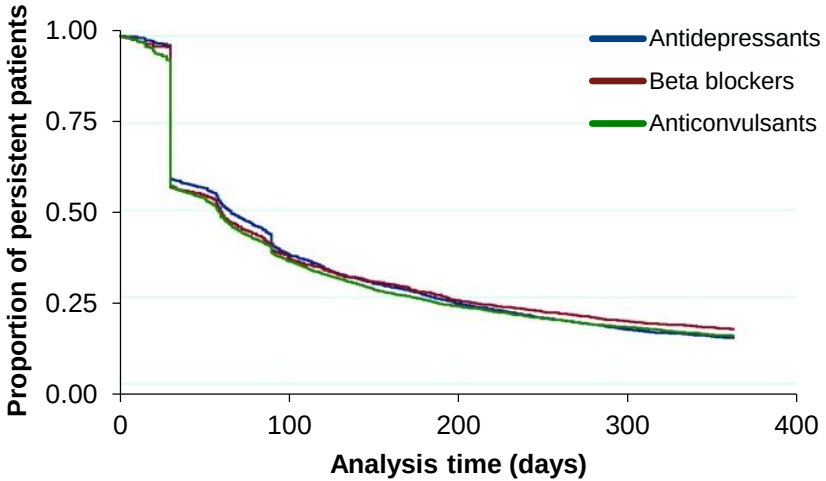
- Effectiveness and speed of onset are considered the most important attributes of preventive migraine treatment (87.3% and 64.4%, respectively), in US patients with migraine[1]
- AHS defines success in migraine prevention by several benefits, including:[2]
  - ≥50% reduction in the frequency of headache or migraine, OR
  - Reduction in migraine-related disability and improvement in functioning, OR
  - Improvement in health-related quality of life and reduction in psychological distress
- Maximal preventive treatment benefit can take 2 to 6 months to be evident[3,4]
  - Benefits of anti-CGRP monoclonal antibodies should be assessed after 3 months for monthly dosing (3 treatments) and 6 months for quarterly dosing (2 treatments)[2]

AHS, American Headache Society

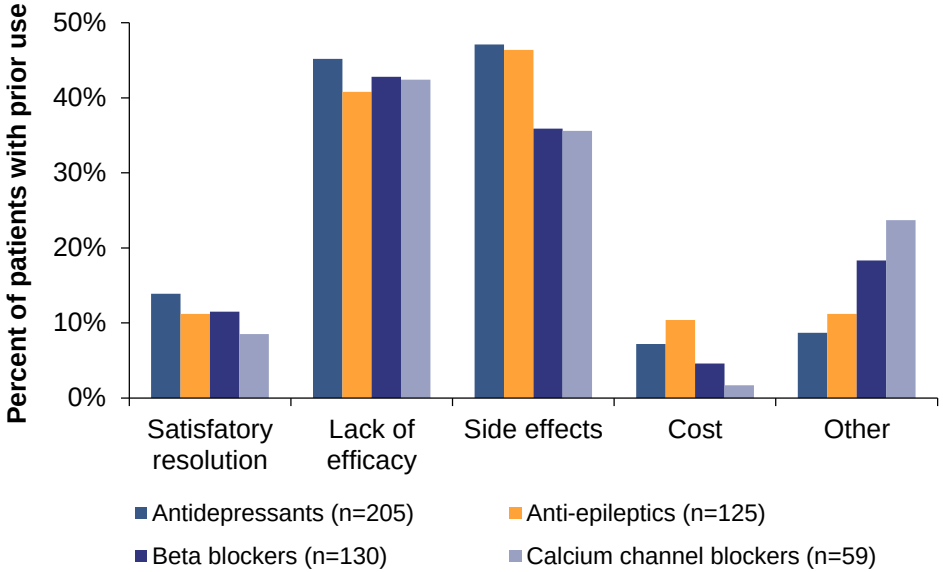
1. Peres MF, et al. *Headache*. 2007. doi: 10.1111/j.1526-4610.2007.00757.x; **2.** American Headache Society. Headache. 2019. doi: 10.1111/head.13456; **3.** Silberstein SD. *Continuum (Minneap Minn)*. 2015. doi: 10.1212/CON.0000000000000199; **4.** American Migraine Foundation. https://americanmigrainefoundation.org/resource-library/understanding-migrainepreventive-treatments/. Accessed March 22, 2019

Persistence with oral migraine prevention is poor due to low efficacy or intolerable side effects[1–4]

- Prophylactic discontinuation up to 12 months from initiation[1]



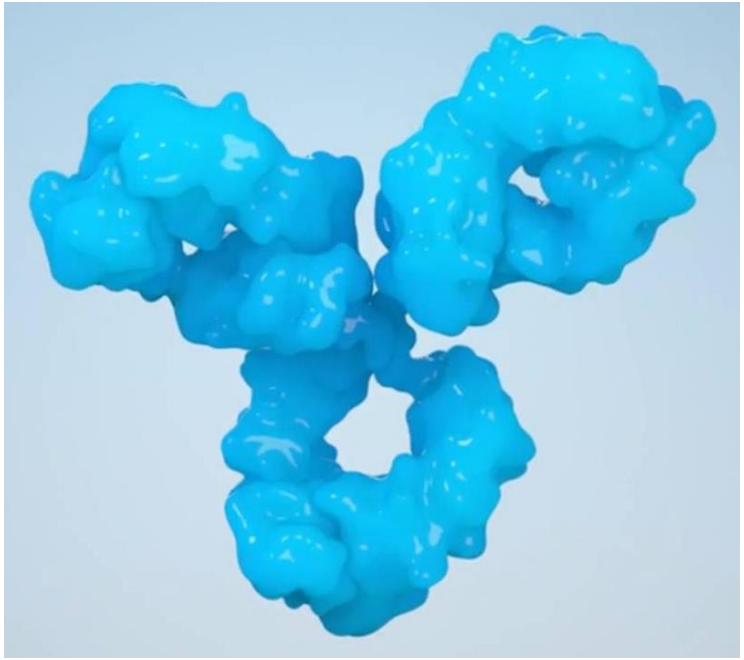
- Patient-reported reasons for discontinuing migraine prophylaxis[2]



1. Hepp Z, Dodick DW, Varon SF, et al. *Cephalalgia*. 2017. doi: 10.1177/0333102416678382; **2.** Blumenfeld AM, Bloudek LM, Becker WJ, et al. *Headache*. 2013. doi: 10.1111/head.12055; **3.** Ford JH, Jackson J, Milligan G, et al. *Headache*. 2017. doi: 10.1111/head.13202; **4.** Woolley JM, Bonafede MM, Maiese BA, Lenz RA. *Headache*. 2017. doi: 10.1111/head.13157.

Molecular design and IV delivery of eptinezumab allows for a rapid preventive effect

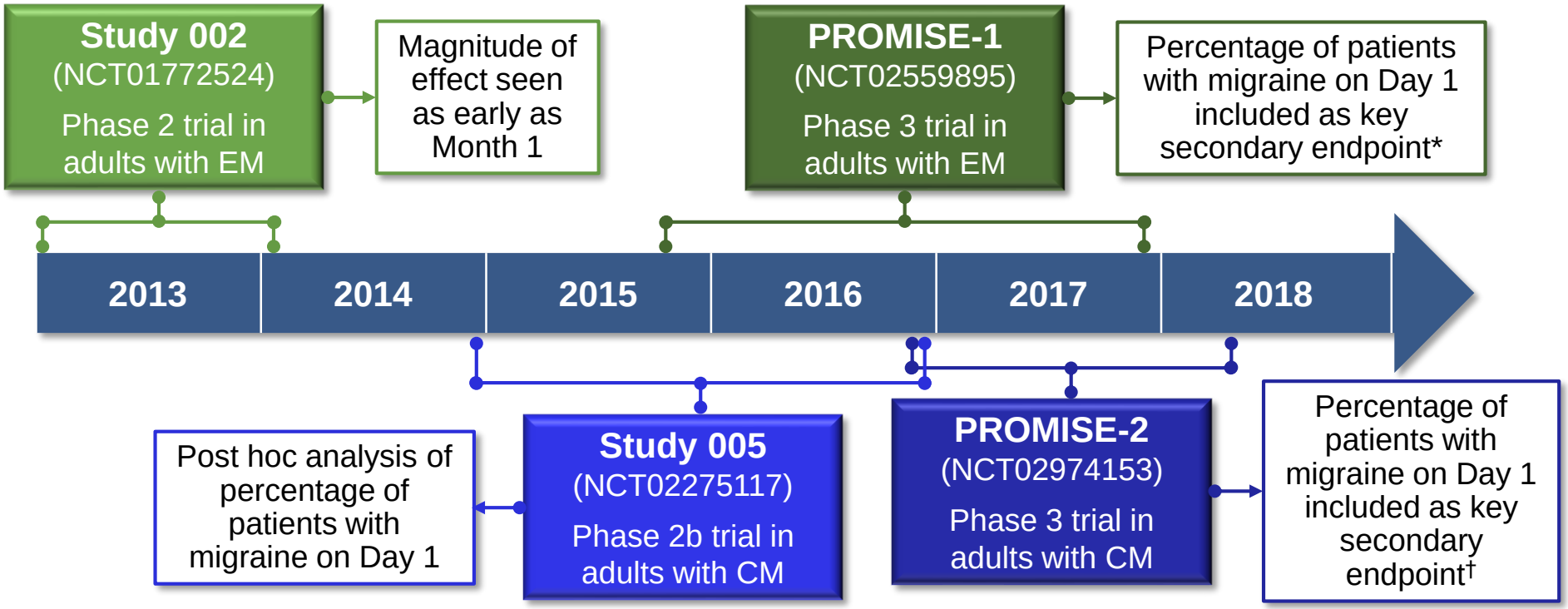
- Humanized monoclonal antibody designed to selectively target the CGRP ligand blocking activation at any calcitonin receptor[1]
- Potent, strong binding (K_D = 4 pM) to CGRP ligand provides sustained interruption of ligand activity[2-4]
- Delivered by quarterly IV infusion, providing immediate C_{max} and 100% bioavailability at the end of infusion[2,5,6]



K_D, equilibrium dissociation constant

1. Vermeersch S, et al. J Pharmacol Exp Ther. 2015. doi: 10.1124/jpet.115.224212; **2.** Latham J, Karasek C, Ojala E, Allison D. Cephalalgia. 2016. doi: 10.1177/0333102416670318; **3.** Monteith D, et al. Front Pharmacol. 2017. doi: 10.3389/fphar.2017.00740; **4.** Alder BioPharmaceuticals. Data on file, 2019; **5.** Baker B, Smith J. *Cephalalgia*. 2015. doi: 10.1177/0333102415581304; **6.** Baker B, Schaeffler B, Cady R, Latham J, Whitaker T, Smith J. Cephalalgia. 2017. doi: 10.1177/0333102417719573

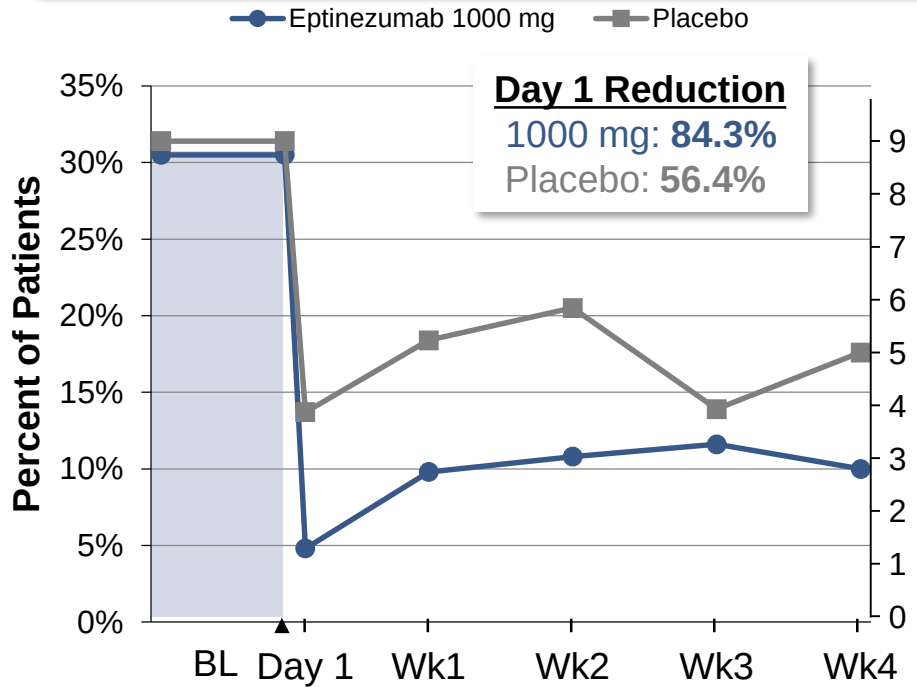
Building evidence to support Day 1 as a key clinical trial endpoint in pivotal phase 3 studies of quarterly dosing of eptinezumab



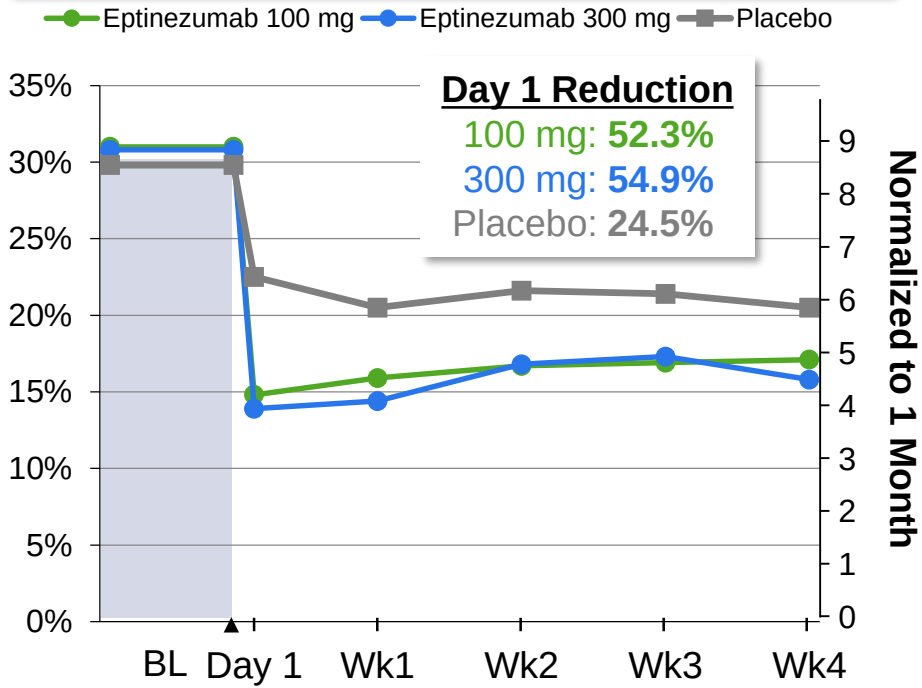
*Included in Series 3 of the decision rule hierarchy of multiplicity procedure, after testing for the primary and subset of key secondary endpoints for 300 mg and 100 mg.
†Included in Series 2 of the decision rule hierarchy of multiplicity procedure, after testing for the primary and subset of key secondary endpoints for 300 mg.

Consistency of rapid onset and sustained preventive effect across trials: Average daily percentage of patients with EM experiencing migraine

Study 002 (Phase 2)*



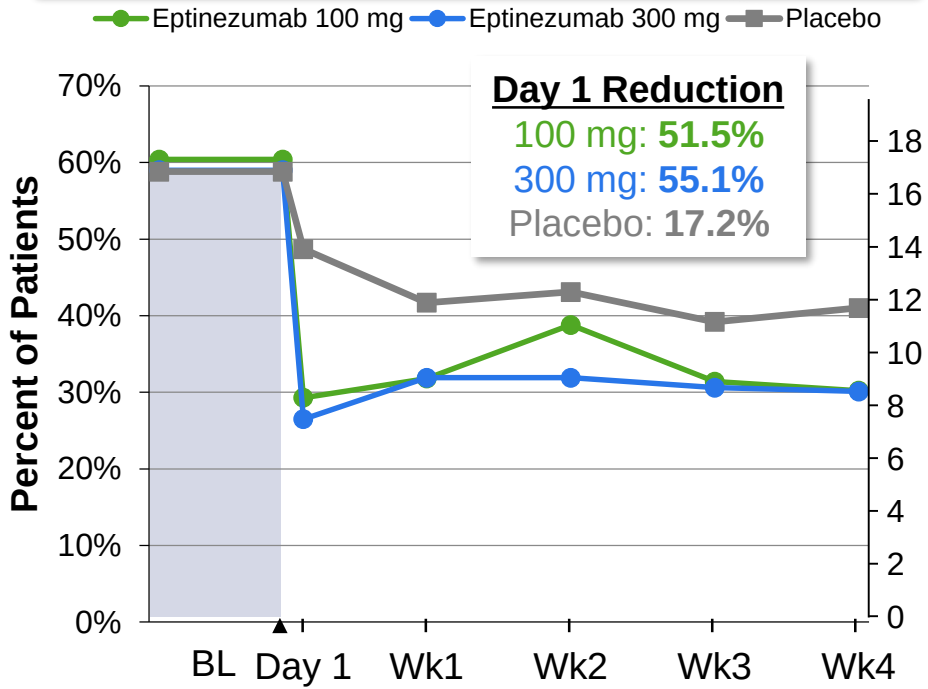
PROMISE-1 (Phase 3)



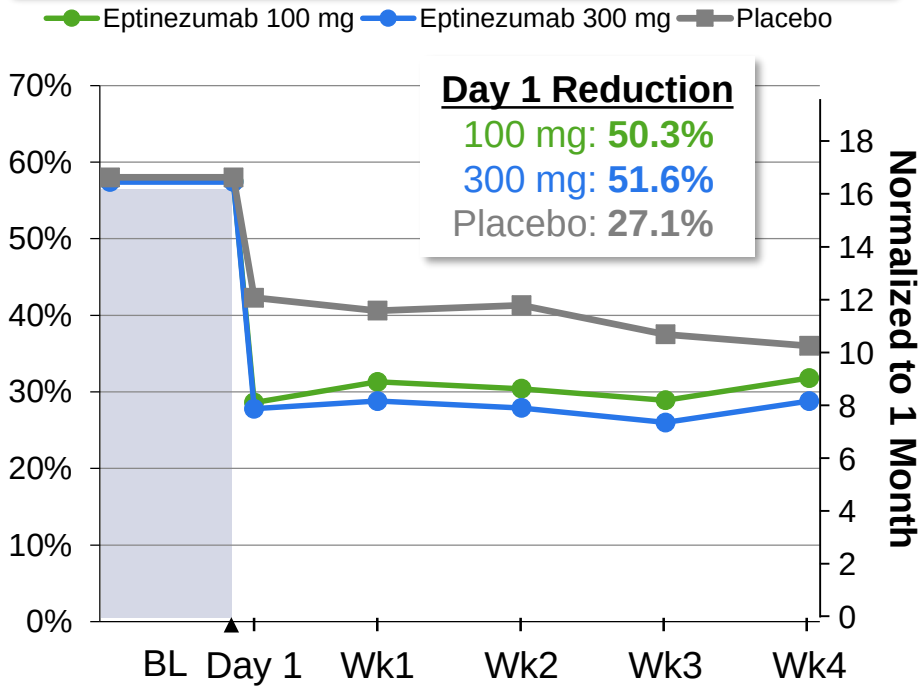
*Post hoc analysis. ▲, infusion; BL, baseline (average over the 28-day screening period); Wk, week.
Values for Weeks 1 through 4 calculated as the average daily percentage of patients with a migraine during that week

Consistency of rapid onset and sustained preventive effect across trials: Average daily percentage of patients with CM experiencing migraine

Study 005 (Phase 2)*



PROMISE-2 (Phase 3)



*Post hoc analysis. ▲, infusion; BL, baseline (average over the 28-day screening period); Wk, week.
Values for Weeks 1 through 4 calculated as the average daily percentage of patients with a migraine during that week

Conclusion

- 100% bioavailability of eptinezumab occurs at the end of infusion, facilitating the potential for a rapid onset of migraine preventive effect
- Observation of Day 1 effect on migraine activity with eptinezumab in phase 2 trials informed the inclusion of Day 1 migraine occurrence as a prespecified key secondary endpoint in phase 3 trials
- Across 4 migraine prevention trials, eptinezumab consistently demonstrated rapid onset of migraine preventive benefit beginning Day 1 after treatment and maintained each week through Month 1
- The response observed during Month 1 was sustained through the first quarterly infusion, and maintained or further increased through subsequent infusions
  - Please see Podium Presentation 003 (PROMISE-1) and Poster 10-006 (PROMISE-2)