# Development of olorinab, a cannabinoid type 2 receptor agonist, for the management of chronic abdominal pain disorders

**Meeting:** Biennial Meeting of the European Society of Neurogastroenterology and Motility (NeuroGastro) 2019, Lisbon, Portugal

**Abstract submission deadline:** Monday, April 15, 2019 – no time given

**Graphic:** 1 figure **(limit: 1 figure, no tables)**

**Presentation type:** Oral or poster

**Topic:** Visceral pain mechanisms

**Presenting/Corresponding author:** *Brett A. English*

**Word Count**: 346/350 max including authors and affiliations, excluding title & figure

Peter D.R. Higgins,[1] Brooks Cash,[2] Kye Gilder,[3] Beatriz Lindstrom,[3] Brett A. English,[3] Stewart Turner,[3] Lin Chang[4]

*[1]University of Michigan, Ann Arbor, MI, USA; [2]McGovern Medical School, Houston, TX, USA; [3]Arena Pharmaceuticals, Inc, San Diego, CA, USA; [4]David Geffen School of Medicine at UCLA, Los Angeles, CA, USA*

**Objectives:** Non–habit-forming therapies with acceptable adverse event (AE) profiles are needed for conditions with persistent abdominal pain. Although non-selective agonists of the cannabinoid type 2 receptor ($CB_2$) exhibit analgesia, their utility is limited by psychoactive effects likely from off-target $CB_1$ activation in the brain. Olorinab (APD371) is a peripherally restricted, selective $CB_2$ agonist in development for abdominal pain in inflammatory bowel

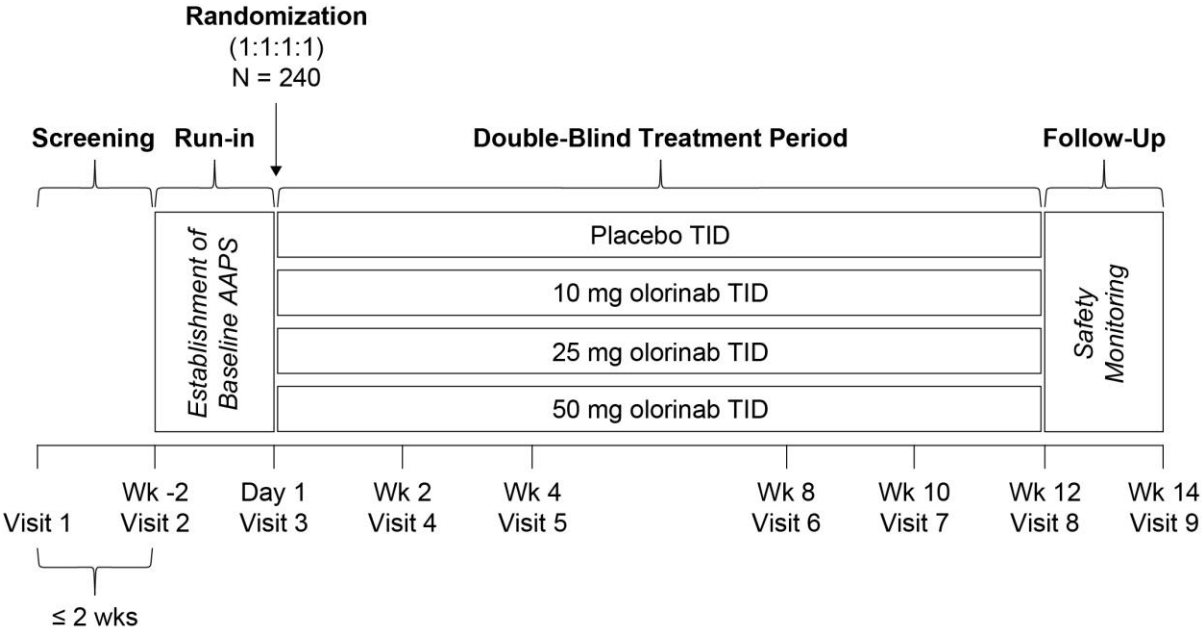
disease (IBD) and irritable bowel syndrome (IBS). Olorinab demonstrated no psychoactive effects in healthy volunteers and was evaluated in a small phase 2a study of abdominal pain in Crohn's disease (CD).

**Methods:** The open-label phase 2a study enrolled adults with quiescent CD experiencing abdominal pain; subjects were randomly assigned 1:1 to 25 or 100 mg oral olorinab 3 times daily (TID) for up to 8 weeks. The primary outcome was safety; exploratory endpoints included change in average abdominal pain score (AAPS; scale 0 [no pain] to 10 [worst pain]) and pain-free days/week.

**Results:** In the phase 2a study (N=14), AAPS was significantly improved in evaluable subjects (n=11) at week 8 and was reduced from Baseline (BL) by -4.6 ($P<0.001$; mean BL, 6.0). Mean pain-free days/week increased from 0 at BL to 2 at week 8 (n=11). AEs were reported in 67% who received 25 mg and 75% who received 100 mg (mostly mild/moderate, none serious; most common: drug hypersensitivity, pain in extremity, hypomagnesaemia). No subjects discontinued because of AEs, and no psychoactive effects were reported.

**Conclusions:** The phase 2a olorinab study provided evidence for visceral analgesia without psychoactive effects in subjects with quiescent CD and abdominal pain. Based on these promising results, a double-blind, placebo-controlled phase 2 study will evaluate the efficacy pharmacokinetics, and safety of olorinab for abdominal pain in adult patients with IBS with constipation or diarrhoea (IBS-C/D; up to 12 weeks of treatment) (Figure).

**Figure. Phase 2 study design of olorinab for abdominal pain in IBS.**




AAPS, average abdominal pain scale; TID, 3 times per day; Wk, week
Notes: The Screening Period may be extended to up to a total of 4 weeks for subjects who consent to colonic biopsy.
On Day 1, subjects will arrive at the study site in the morning and will stay for an overnight observation period.