Ozanimod in UC

- First S1P therapy FDA-approved for UC[1]; phase 3 trial for CD underway[2]
  - S1P modulators block lymphocytes from entering circulation; anti-inflammatory[3]
  - Ozanimod selective for $S1P_{1,5}$ receptors[3]

10-WEEK INDUCTION PHASE[3]		
Endpoints	**Ozanimod* (1 mg/day; oral) (n = 429)**	**Placebo (n = 216)**
Clinical Remission (Primary)	**18.4%**	**6.0%**
Clinical Response	47.8%	25.9%
Endoscopic Improvement	27.3%	21.1%
Histologic-Endoscopic Mucosal Healing	12.6%	3.7%

MAINTENANCE PHASE WEEKS 10-52[3]		
Endpoints	**Ozanimod* (1 mg/day; oral) (n = 230)**	**Placebo (n = 227)**
Clinical Remission (Primary)	**37.0%**	**18.5%**
Clinical Response	60.0%	41.0%
Endoscopic Improvement	45.7%	26.4%
Histologic-Endoscopic Mucosal Healing	29.6%	14.1%
Maintenance of Remission	52.0%	29.0%
Glucocorticoid-free Remission	31.7%	16.7%
Durable Remission	17.8%	9.7%

*Significant difference between ozanimod and placebo groups, $P \leq 0.003$ for all endpoints.
S1P, sphingosine -1-phosphate.
1. ZEPOSIA® (ozanimod). Prescribing information. Bristol-Myers Squibb Company; 2023; 2. Clinicaltrials.gov. NCT03464097; 3. Sandborn WJ, et al. *N Engl J Med.* 2021;385(14):1280-91.

Etrasimod in UC

UPDATE:
Approved by FDA for UC October 13, 2023.

- Selective for $S1P_{1,4,5}$ receptors
- Results from 2 trials: Elevate 12 and Elevate 52 in UC
  - Unique "treat-through" design: all patients in induction phase remain blinded and continue through maintenance phase, regardless of response to drug at week 12

52-WEEK ETRASIMOD INDUCTION AND MAINTENANCE TRIAL								
Efficacy Endpoints	**Elevate 12**				**Elevate 52**			
	Week 12		**Week 52**		**Week 12**		**Week 52**	
	Etrasimod* (2 mg, n = 238)	Placebo (n = 116)	Etrasimod* (2 mg, n = 238)	Placebo (n = 116)	Etrasimod† (2 mg, n = 289)	Placebo (n = 144)	Etrasimod† (2 mg, n = 289)	Placebo (n = 144)
Clinical remission (primary)	**26%**	**15%**	**---**	**---**	**28%**	**8%**	**33%**	**8%**
Endoscopic improvement	--	--	33%	19%	37%	17%	39%	13%
Symptomatic remission	--	--	48%	29%	46%	22%	44%	19%
Endoscopic improvement – histological remission	--	--	17%	9%	23%	6%	27%	10%

*$P \leq 0.003$ for all endpoints for Elevate 12. †$P \leq 0.0001$ for all endpoints for Elevate 52.
S1P, sphingosine -1-phosphate.
Sandborn WJ, et al. *Lancet*. 2023;401(10383):1159-71.

S1P Receptor Modulators Ozanimod and Etrasimod in UC — Safety

42-WEEK OZANIMOD MAINTENANCE PERIOD[1]		
Safety Endpoints	**Ozanimod (n = 230)**	**Placebo (n = 227)**
Serious adverse events	5.2%	7.9%
Discontinuation due to adverse event	1.3%	2.6%
Serious infection	0.9%	1.8%
Hypertension	1.7%	1.3%
Hypertensive crisis	0.4%	0.4%
Macular edema	0	0.4%
Absolute lymphocyte count		
<200 cells per mm^3	0	2.2%
<500 cells per mm^3	43.5%	1.8%
Elevated alanine aminotransferase		
≥ 2x ULN	13.9%	5.3%
≥ 3x ULN	3.0%	1.8%
≥ 5x ULN	0.9%	0.4%

52-WEEK ETRASIMOD TRIALS[2]				
Safety Endpoints	**ELEVATE UC 12**		**ELEVATE UC 52**	
	Etrasimod (n = 238)	**Placebo (n = 116)**	**Etrasimod (n = 289)**	**Placebo (n = 144)**
Serious adverse events	3%	2%	7%	6%
Discontinuation due to adverse event	5%	1%	4%	5%
Serious infections	0	0	3%	4%
Hypertension	1%	1%	3%	1%
Sinus bradycardia	2%	0	0	0
Bradycardia	1%	0	1%	0
Atrioventricular block, 1st deg.	<1%	0	<1%	0
Atrioventricular block, 2nd deg.	0	0	<1%	0
Macular edema	<1%	<1%	<1%	0

- Low levels of cancer, serious and opportunistic infections, and macular edema[1,2]
- Almost 50% have reduced lymphocyte levels[1,2]
- Liver dysfunction in ozanimod group[1]
- Cardiac heart rate or conduction aberrations associated with first dose[1,2]

ULN, upper limit of normal.

1. Sandborn WJ, et al. *N Engl J Med.* 2021;385(14):1280-91; 2. Sandborn WJ, et al. *Lancet*. 2023;401(10383):1159-71.