Efficacy and Safety of Vidofludimus Calcium (IMU-838) in Patients with Moderately to Severely Active Ulcerative Colitis (UC): Results from the Prospective Placebo-Controlled Phase 2 CALDOSE-1 Trial

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Abstract # AS-UEG-2023-01648

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Disclosure of Conflicts of Interest

- GH: served as advisor for Abbvie, Alimentiv, Astrazeneca, Bristol Meiers Squibb, Boehringer Ingelheim, Celltrion, Eli Lilly, Galapagos, Glaxo Smith Kline, Immunic, Johnson and Johnson, Pfizer, Polpharm, Prometheus laboratories, Procise diagnostics, Roivant, Samsung Bioepis, Takeda, Tillotts, Ventyx; received speaker fees from Abbvie, Boehringer, Eli Lilly, Johnson and Johnson, Pfizer, Takeda, Tillotts.
- SR is a former employee of the trial sponsor.
- DV is a shareholder and employee of the trial sponsor, and a holder of patents for the drug under investigation.
- HK is a shareholder and employee of the trial sponsor, and a holder of patents for the drug under investigation.
- AM is a shareholder and employee of the trial sponsor, and a holder of patents for the drug under investigation.

Vidofludimus Calcium Targeted to Be a Precision Medicine to Inhibit Inflammation of the Bowel at Its Source

Preserves Normal Immune Cell Function and Numbers

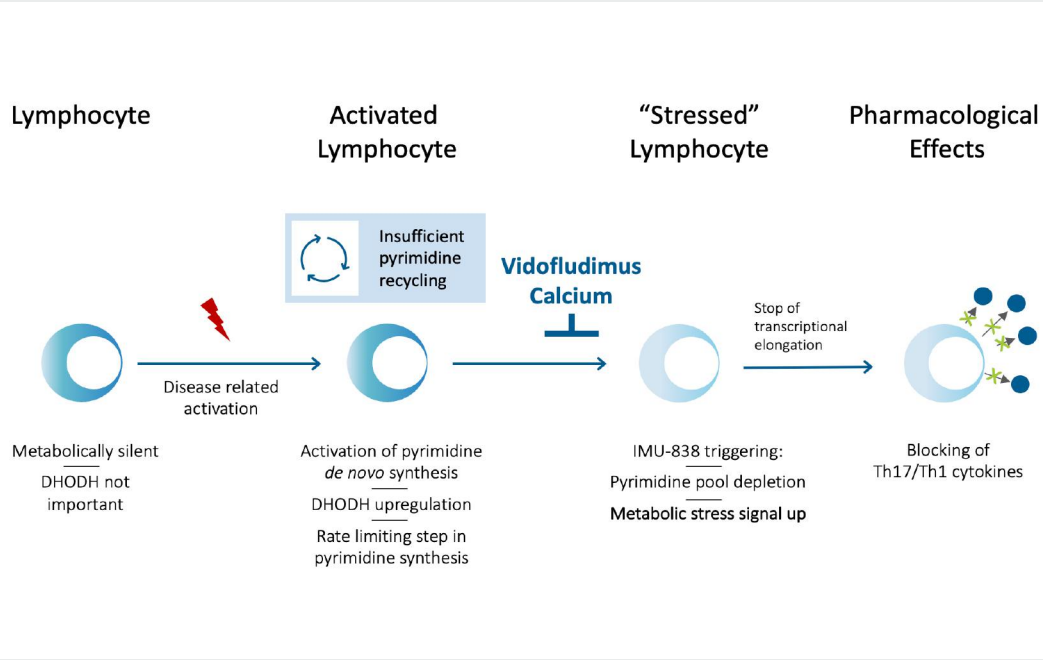
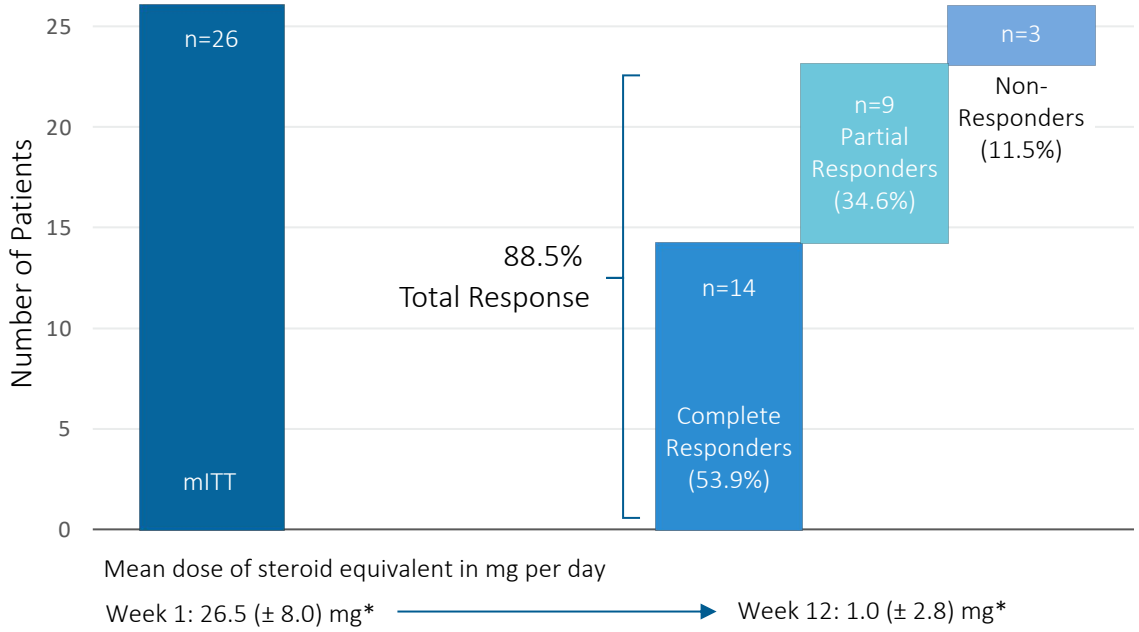


Illustration adapted from Tan et al., 2016, Mol Cell 62 / DHODH: dihydroorotate dehydrogenase

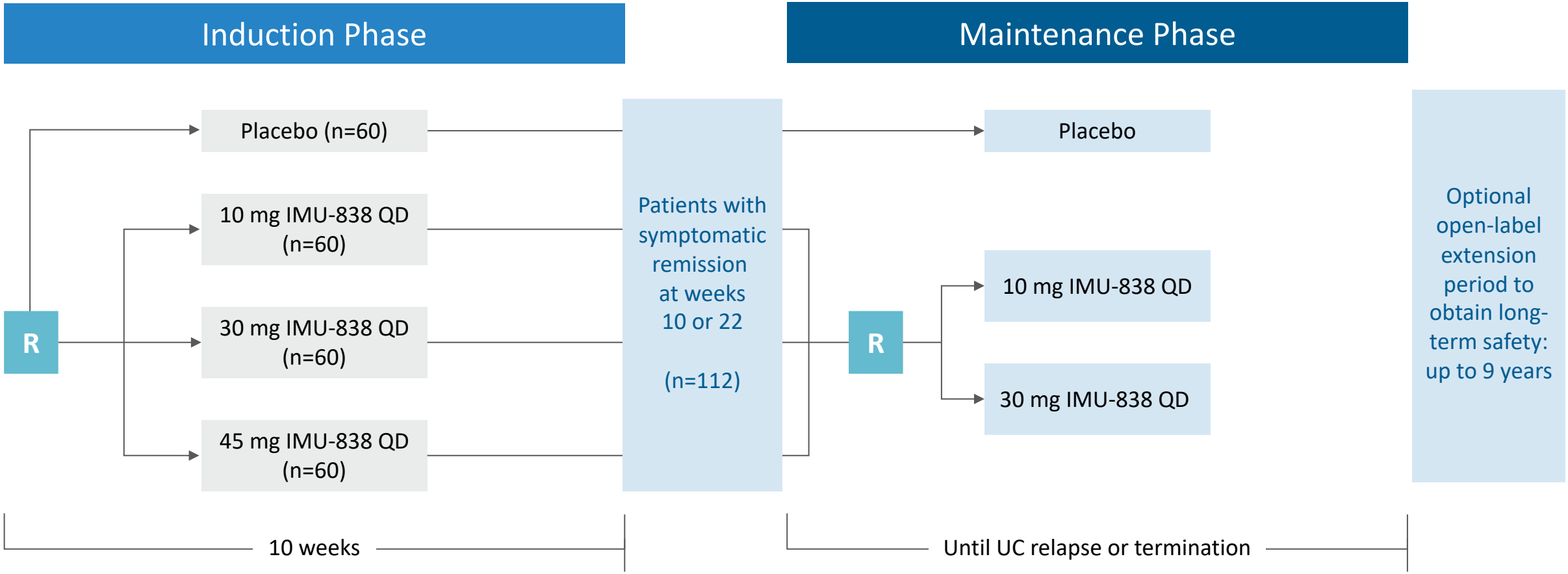
ENTRANCE Study Showed Activity of Vidofludimus in IBD



Herrlinger et.al., 2011, Gastroenterology 140:588
Includes patients with steroid dependent IBD after failing at least 2 withdrawing attempts and on daily steroid doses ≥20mg
QD: quaque die = once-daily; mITT: modified intent to treat population

CALDOSE-1: Phase 2b Clinical Trial in Ulcerative Colitis (UC)

NCT03341962



Total number of patients randomized: N=263

Final analysis induction phase after 10 weeks

Final analysis maintenance phase after 50 weeks

R: randomization; QD: quaque die = once-daily

Symptomatic remission: patient-reported symptomatic remission contains stool frequency Mayo subscore of 0 or 1 and rectal bleeding Mayo score of 0

CALDOSE-1: Phase 2b Clinical Trial in Ulcerative Colitis (UC)
NCT03341962

Patient Population

- Male and female patients, aged 18 to 80 years
- UC diagnosed more than 3 months before screening
- Previous treatment failure with immuno-modulators, steroids or biologicals
- Active symptoms defined as a Mayo stool frequency score of ≥2 and a modified Mayo endoscopy subscore of ≥2 at the screening flexible sigmoidoscopy (independent central reader)

A Induction Phase

- Concomitant use of corticosteroids was allowed:
  - At doses ≤20 mg prednisolone equivalent
  - Steroid dose MUST remain stable for entire induction phase
- Approximately 50% of patients had concomitant corticosteroids and were well balanced between groups due to stratification during randomization in induction phase

B Maintenance Phase

- Re-randomization of vidofludimus calcium patients to 10 and 30 mg doses (independent of their induction phase treatment assignments)
- Placebo patients who achieved symptomatic remission during induction phase “sham randomized” to continue on placebo
- Forced corticosteroids tapering required at the start of the maintenance phase

Primary Endpoint

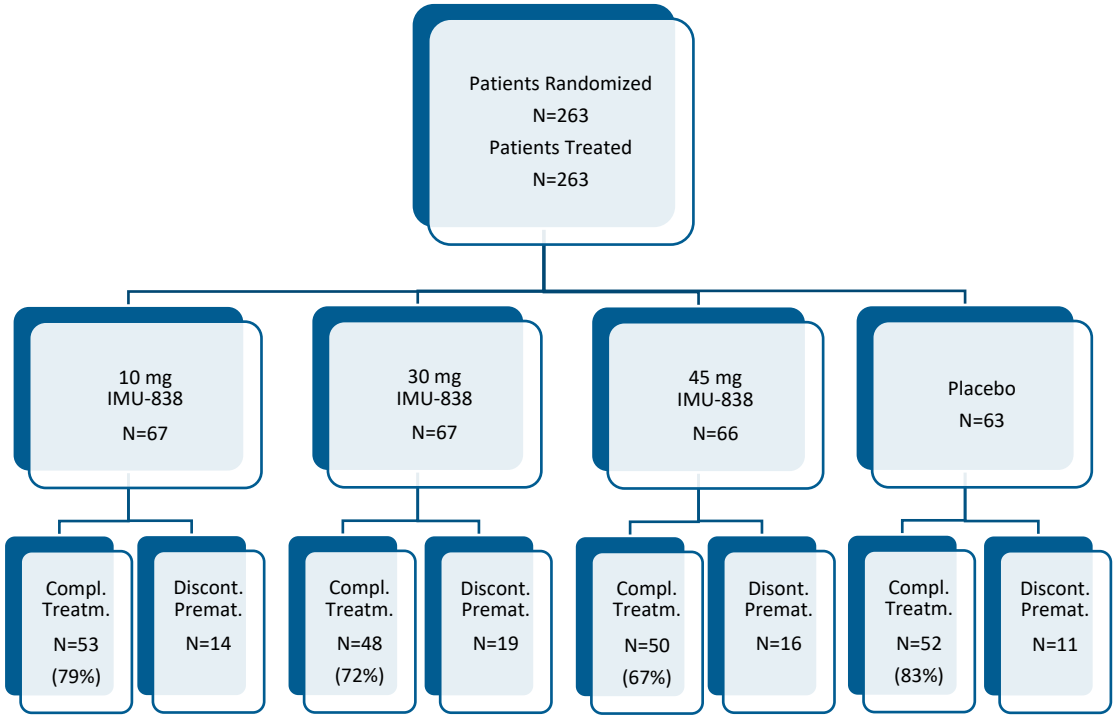
Composite endpoint of clinical remission: proportion of patients at week 10 with

- symptomatic remission, and
  (Mayo rectal bleeding subscore = 0, Mayo stool frequency subscore of 0 or 1)
- endoscopic healing
  (Modified Mayo endoscopy subscore of 0 or 1)

Induction Phase: Patient Characteristics and Prior Treatment History

Baseline Characteristics			Placebo N=64	10 mg IMU-838 N=67	30 mg IMU-838 N= 66	45 mg IMU-838 N= 66
Median age (years)			38.5	40.0	41.0	40.5
Male (N in %)			33 (51.6%)	35 (52.5%)	40 (60.6%)	40 (60.6%)
Race		White	62	64	66	63
		Other	2	3	0	3
Severity of disease*			15 (23.8%)	23 (34.3%)	15 (22.4%)	21 (31.8%)
Full Mayo score at baseline			9.1	9.0	9.1	9.1
C-reactive protein (mg/L)			10.4	10.9	10.7	11.0
Calprotectin (mg/kg)			1252.2	1097.6	1135.3	1750.2
Patients with concomitant steroid use at randomization			32 (51%)	34 (51%)	35 (52%)	30 (46%)
Prior UC treatment before study	Biologics	No	52	53	56	55
		Yes	11	14	11	11
	Corticosteroids	No	2	2	3	6
		Yes	61	65	64	60

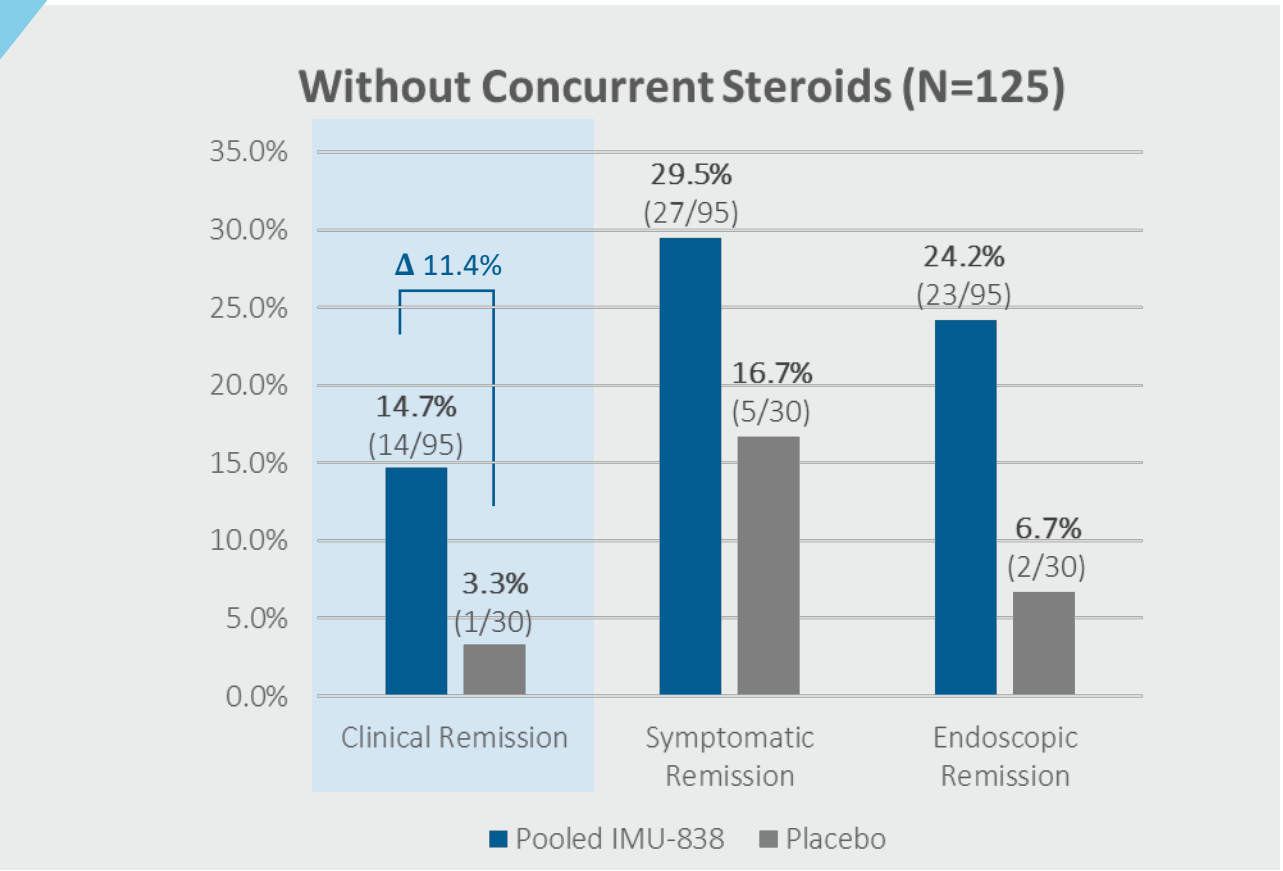
Patients Per Treatment Group

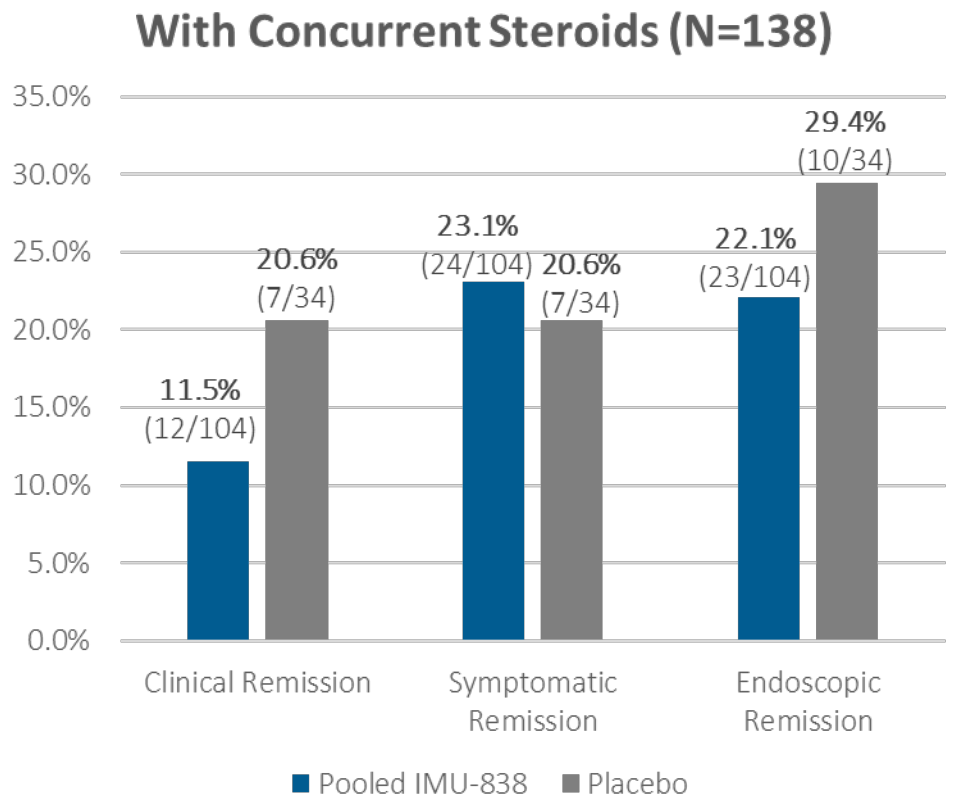


Compl Treatm: completed induction phase
Disc Premat: discontinued treatment without completing the end of induction visit.

C-reactive protein (CRP) = group averages are given as arithmetic means * Disease severity is rated by investigator and not based on Mayo score.
1 patient received erroneously 30 mg IMU-838 instead of placebo and was included in the 30 mg IMU-838 group for the safety analysis, but in the placebo group for the efficacy assessments (as randomized analysis).

Induction Phase: Clinical Remission for UC Patients Without and With Concomitant Corticosteroid





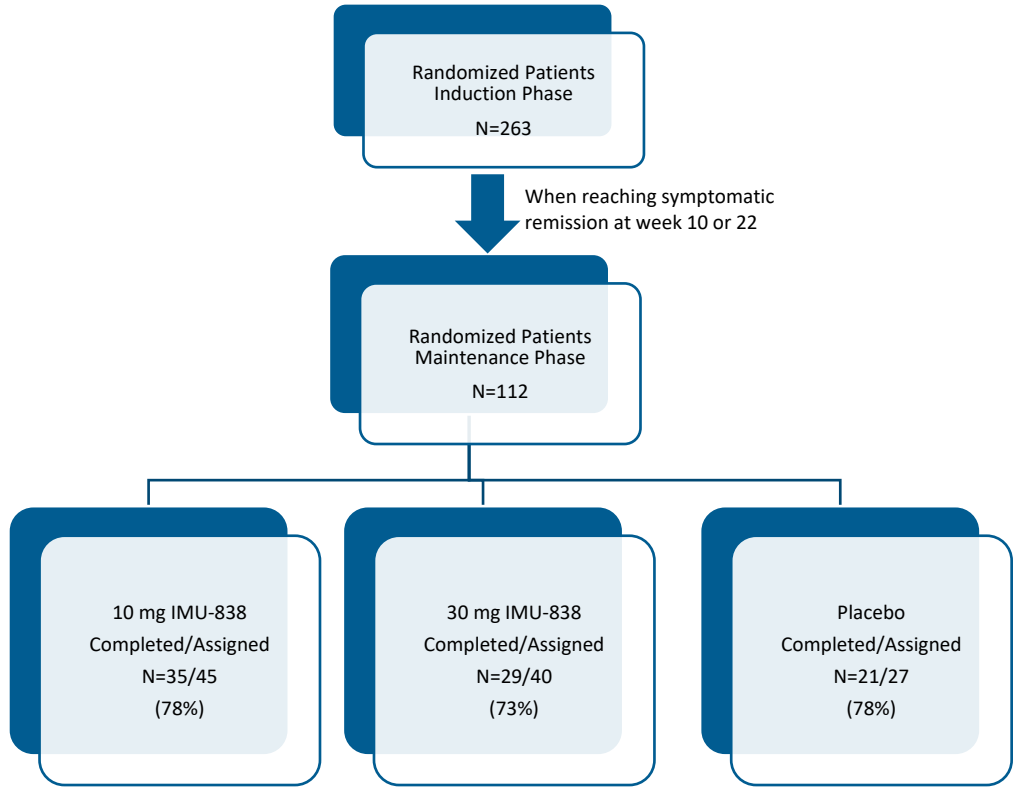
The graphs use the concurrent use of corticosteroids, as used as stratification factor for randomization provided by the investigator, not actual use of concurrent corticosteroids. However, actual steroid use does not differ substantially.
Data display ITT population of both biologic-naïve and -experienced patients. Pooled vidofludimus calcium data contain all data from 10 mg (no steroids n=33, steroids n=34), 30 mg (no steroids n=32, steroids n=34), 45 mg IMU-838 (no steroids n=30, steroids n=36). Placebo data: no steroids n=30, steroids n=34.
Clinical remission: achieving both symptomatic remission and endoscopic remission, Symptomatic remission: Mayo rectal bleeding subscore of 0, and Mayo stool frequency subscore of 0 or 1, Endoscopic remission: Modified Mayo endoscopy subscore of 0 or 1

Maintenance Phase: Patient Characteristics and Prior Treatment History

Characteristics			Placebo N=27	10 mg IMU-838 N=45	30 mg IMU-838 N= 40
Mean age (years)			40.1	39.7	43.8
Male (N in %)			18 (66.7%)	30 (66.7%)	15 (37.5%)
Race		White	26	45	40
		Other	1	0	0
Mayo PRO-2 score at baseline maintenance			0.7	0.8	0.9
C-reactive protein (mg/L)			1.4	5.1	4.9
Calprotectin (mg/kg)			742.5	403.9	971.9
Concomitant steroids at baseline maintenance			17 (63%)	22 (49%)	22 (54%)
Prior UC treatment before study	Biologics	No	23	43	38
		Yes	4	2	2
	Corticosteroids	No	0	3	2
		Yes	27	42	38

C-reactive protein (CRP) = group averages are given as arithmetic means
Mayo PRO-2 score = Mayo patient-reported outcome score of stool frequency and rectal bleeding score

Patients Per Treatment Group

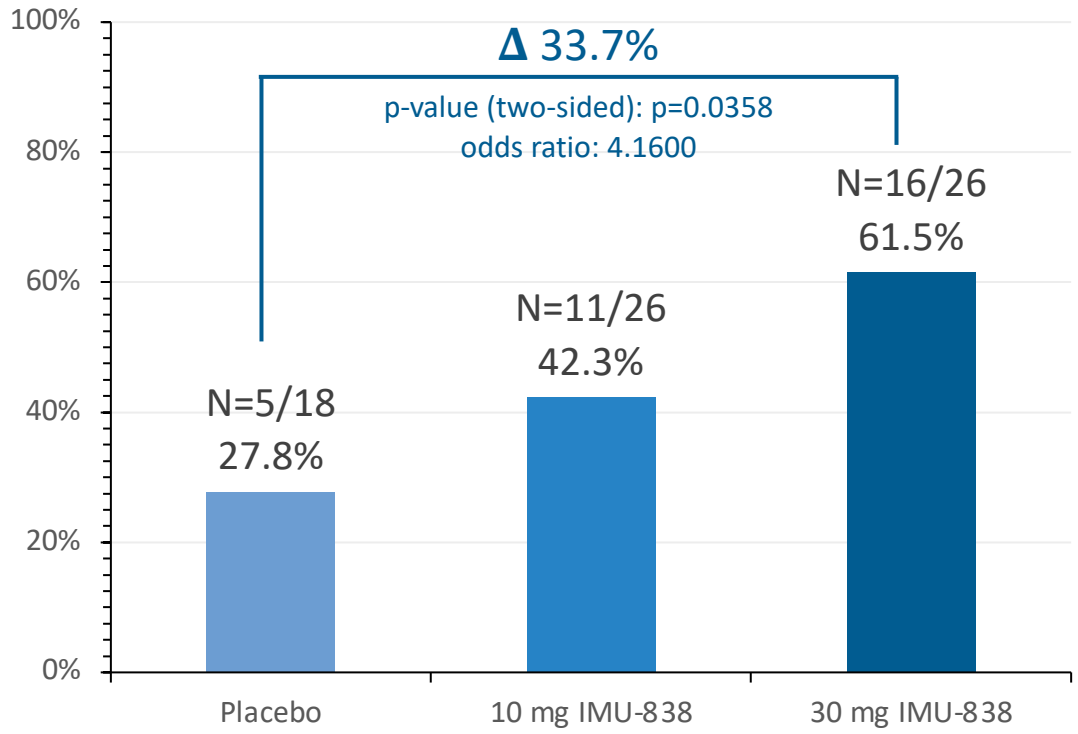


Completed the maintenance phase means the end of maintenance phase visit was completed (including endoscopy).

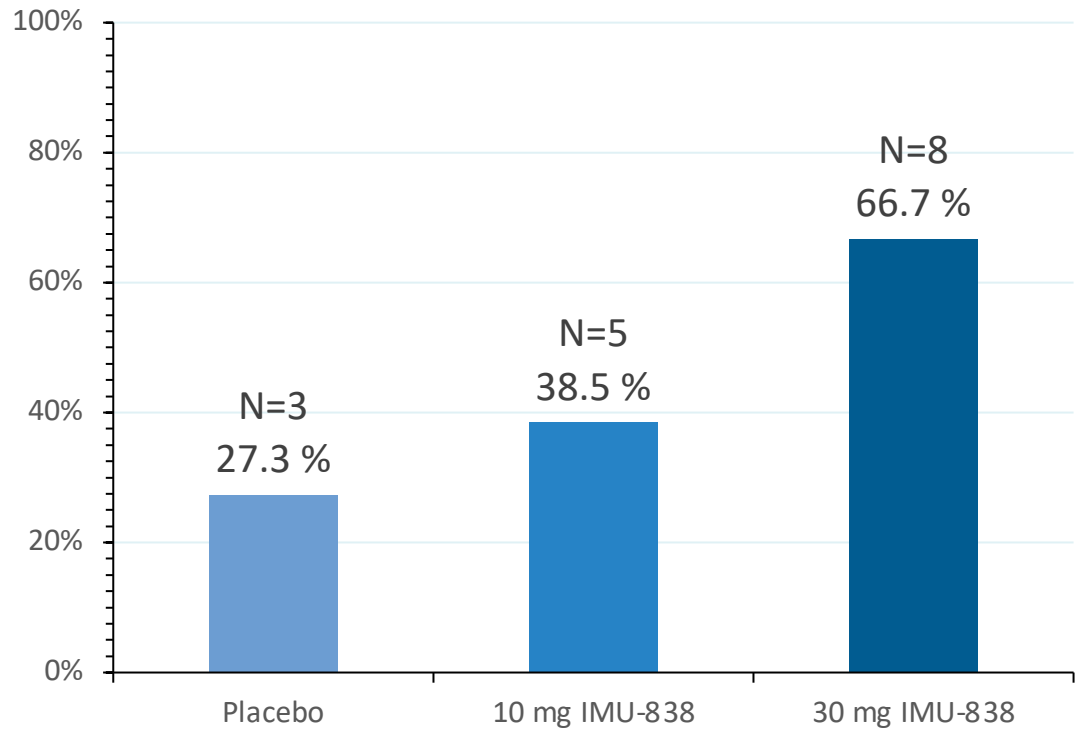
Maintenance Phase: Clinical Remission at Week 50

Vidofludimus Calcium Superior to Placebo

Dose-Linear Increase in Clinical Remission at Week 50 for Vidofludimus Calcium



Steroid-Free Clinical Remission of Induction Steroid Subgroup at Week 50

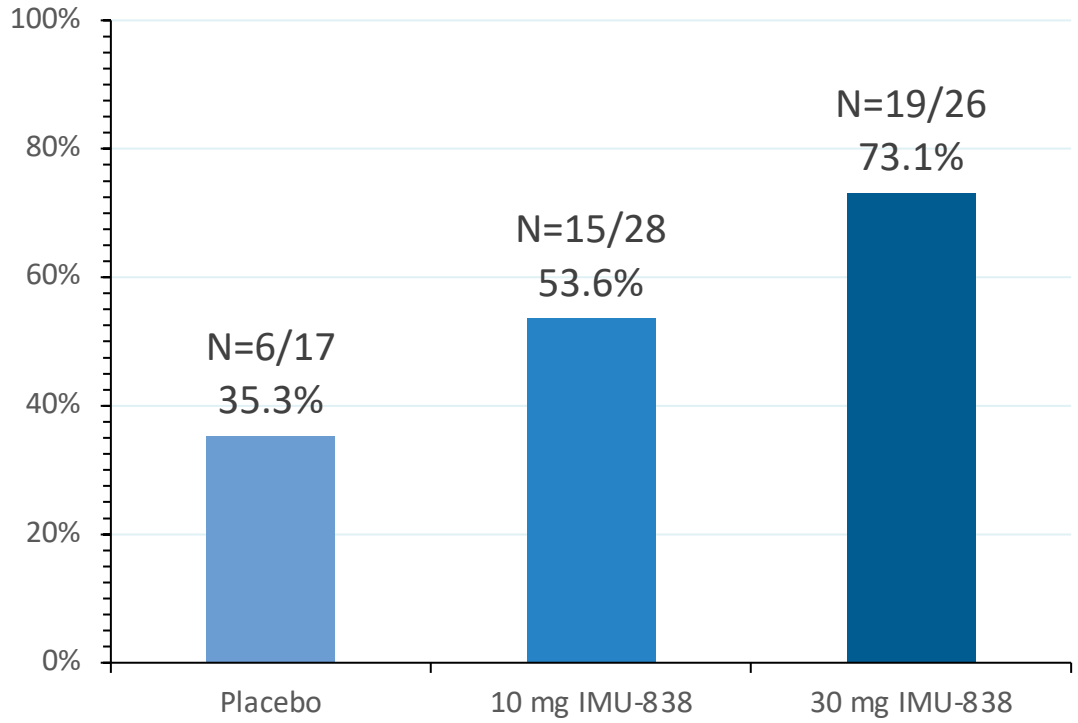


Full Analysis Set MP: all patients randomized into maintenance phase
Clinical remission: composite of patient-reported symptomatic remission (stool frequency Mayo subscore of 0 or 1, rectal bleeding Mayo score of 0) and modified Mayo endoscopy subscore of 0 or 1

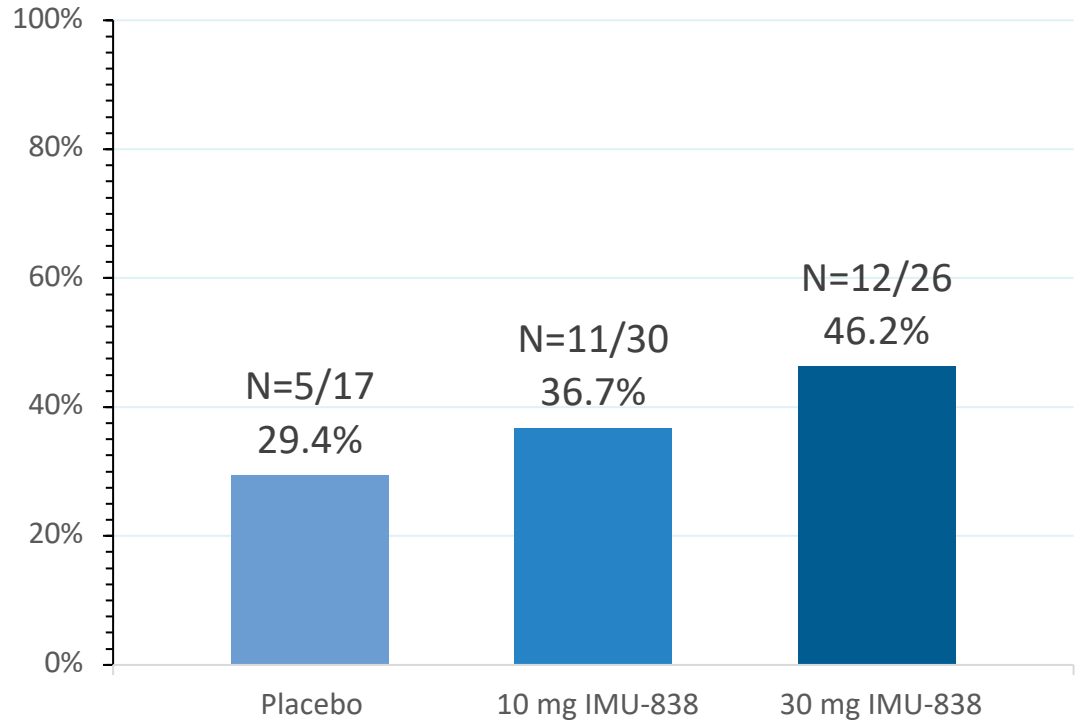
Maintenance Phase: Endoscopic Healing at Week 50

Vidofludimus Calcium Superior to Placebo

Endoscopic Healing at Week 50



Microscopic Healing at Week 50



Full Analysis Set MP: all patients randomized into maintenance phase
Endoscopic healing: modified Mayo endoscopy subscore of 0 or 1; microscopic healing with Geboes score of 2B.0 or better

Maintenance Phase: Incidence of TEAEs Comparable in Both 10 mg and 30 mg Vidofludimus Calcium Groups To Placebo Group

Number of patients with TEAEs, serious TEAEs, and TEAEs of special interest
Safety Set$_{MP}$ (N_{PBO} = 27, N_{10} = 45, N_{30} = 40)

	Placebo		10 mg IMU-838		30 mg IMU-838		Total	
	TEAE N (n)	TEAE (%)	TEAE N (n)	TEAE (%)	TEAE N (n)	TEAE (%)	TEAE N (n)	TEAE (%)
TEAEs	**12(24)**	**44.4%**	**16(26)**	**35.6 %**	**16(33)**	**40%**	**44(83)**	**39.3%**
Serious TEAEs	1(1)	3.7%	3(3)	6.7%	2(2)	5%	6(6)	5.4%
TEAEs of special interest	1(1)	3.7%	0	0.0%	2(2)	5%	3(3)	2.7%
Renal TEAEs	2(2)	7.4%	1(1)	2.2%	2(5)	5%	5(8)	4.5%
Liver TEAEs	1(4)	3.7%	1(1)	2.2%	0	0.0	2(2)	1.8%

Safety set maintenance phase: all patients who were randomized into maintenance phase and received at least one dose of study drug
TEAE of special interest are defined as red blood cells urine positive, hematuria, or retroperitoneal pain
TEAE: treatment-emergent adverse event; MP: maintenance phase; PBO: placebo; N: number of patients; n: number of events

Maintenance Phase: Adverse Events of Interest

No Increase in Liver Events Observed as Compared to Placebo

		Placebo		10 mg IMU-838		30 mg IMU-838		Total	
		TEAE N (n)	TEAE (%)	TEAE N (n)	TEAE (%)	TEAE N (n)	TEAE (%)	TEAE N (n)	TEAE (%)
Hepatobiliary disorders	Cholecystitis	0	0	1(1)	2.2%	0	0	1(1)	0.9%
Investigations	Aspartate aminotransferase increased	1(1)	3.7%	0	0	0	0	1(1)	0.9%
	Gamma-glutamyltransferase increased	1(1)	3.7%	0	0	0	0	1(1)	0.9%
	Hepatic enzyme increased	1(2)	3.7%	0	0	0	0	1(1)	0.9%
	Total	**1(4)**	**3.7%**	**1(1)**	**2.2%**	**0**	**0**	**2(5)**	**1.8%**

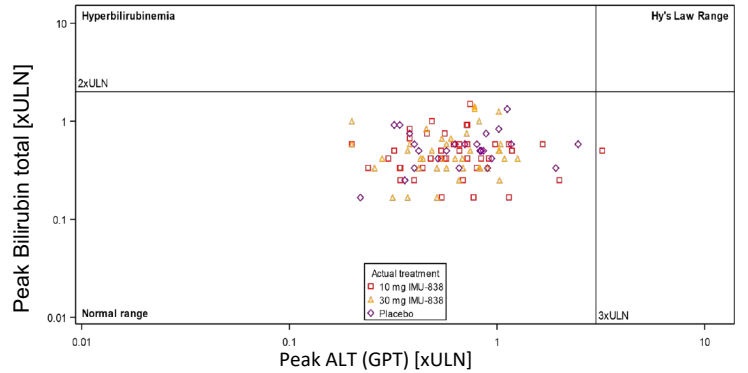
No Increase in Renal Events Observed as Compared to Placebo

		Placebo		10 mg IMU-838		30 mg IMU-838		Total	
		TEAE N(n)	TEAE (%)	TEAE N(n)	TEAE (%)	TEAE N(n)	TEAE (%)	TEAE N(n)	TEAE (%)
Investigations	Blood creatinine increased	1(1)	3.7%	0	0	0	0	1(1)	0.9%
	Blood urine present	0	0	1(1)	2.2%	0	0	1(1)	0.9%
	Red blood cells urine positive	1(1)	3.7%	0	0	0	0	1(1)	0.9%
Renal and urinary disorders	Hematuria	0	0	0	0	2(2)	5%	2(2)	1.8%
	Ketonuria	0	0	0	0	1(1)	2.5%	1(1)	0.9%
	Nephrolithiasis	0	0	0	0	1(1)	2.5%	1(1)	0.9%
	Proteinuria	0	0	0	0	1(1)	2.5%	1(1)	0.9%
	Total	**2(2)**	**7.4%**	**1(1)**	**2.2%**	**2(5)**	**5%**	**5(8)**	**4.5%**

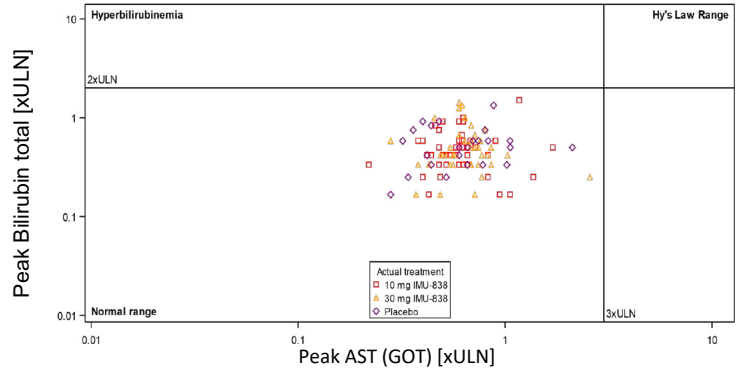
No Hy's Law Cases

Safety Analysis Set$_{MP}$ (N_{PBO} = 27, N_{10} = 45, N_{30} = 40)

Hy's Law Plot: Alanine Aminotransferase (ALT)

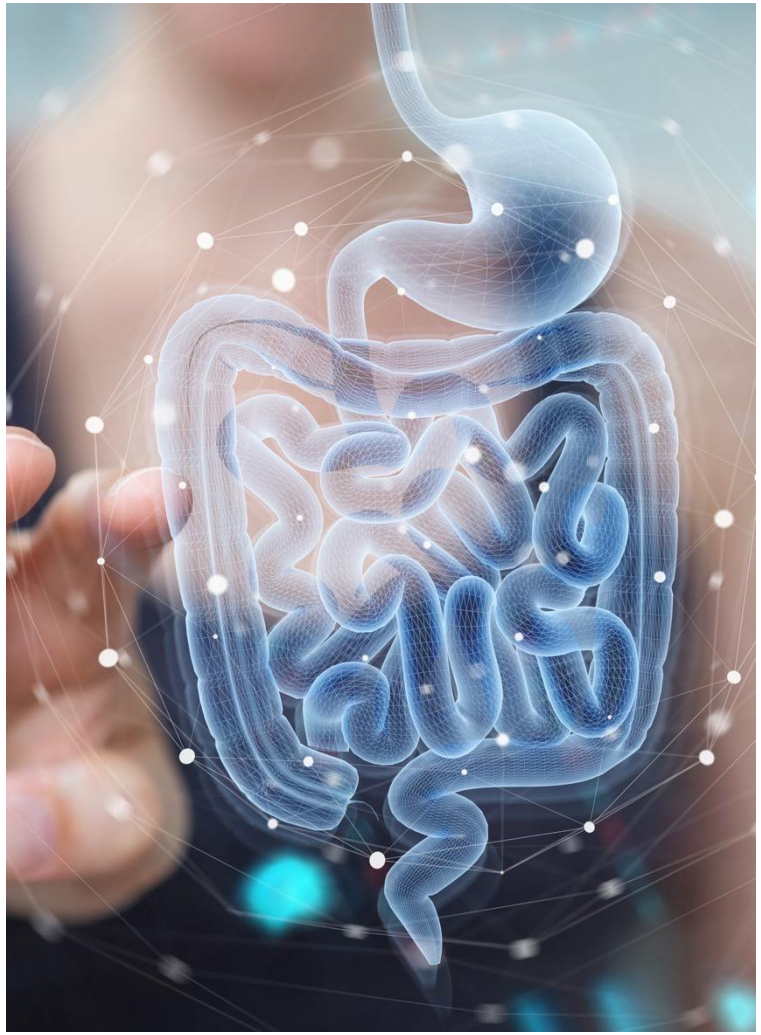


Hy's Law Plot: Aspartate Aminotransferase (AST)



Safety set maintenance phase: all patients who were randomized into maintenance phase and received at least one dose of study drug
Only TEAEs with predetermined preferred terms related to liver / renal function within Investigations and Hepatobiliary / Renal and Urinary Disorders (terms selected by Sponsor before unblinding of study) are displayed.
TEAE: treatment-emergent adverse event; N: number of patients; n: number of events; MP: maintenance phase; PBO: placebo; ULN: upper limit of normal

Phase 2b CALDOSE-1 Trial in Ulcerative Colitis: Summary



- Induction Phase: primary endpoint of induction phase not achieved due to an unexpected interference between vidofludimus calcium and concurrent use of corticosteroids
- Maintenance Phase: results confirm that vidofludimus calcium provides a benefit regarding clinical remission, as compared to placebo, in UC patients without concurrent use of corticosteroids
  - At week 50, a higher proportion of patients on 30 mg vidofludimus calcium once-daily achieved clinical remission compared to placebo (p=0.0358, exploratory analysis)
  - Vidofludimus calcium also numerically more effective than placebo for the other endpoints, such as endoscopic healing, histological healing and steroid-free clinical remission
  - For most efficacy endpoints, dose-linear response observed for 10 mg and 30 mg of vidofludimus calcium
- Safety and Tolerability: vidofludimus calcium in UC patients was comparable to placebo across induction and maintenance phases and in line with prior data sets in other patient populations (relapsing and progressive multiple sclerosis)

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Immunic THERAPEUTICS

Thank you to all investigators and patients!