Table SI. Targeted therapies for treating UC in clinical trials.

First author, year	Target	Drug	Application	Efficacy summary	Clinical status	(Ref.)
Croft *et al*, 2021	TNF-α	Adalimumab	Children aged 4-17 years with moderate-to-severe ulcerative colitis	Clinical remission: 8 weeks: 43-60% (different dose induction) 52 weeks: 29% (standard-dose maintenance adalimumab group), 37% (pooled adalimumab groups)	Phase Ⅲ	(39)
Feagan *et al*, 2023	TNF-α	Golimumab	Moderately to severely active UC	Clinical response: 12 weeks: 61%	Phase II	(40)
Feagan *et al*, 2023	IL-12/23	Guselkumab	Moderately to severely active UC	Clinical response: 12 weeks: 75%	Phase II	(40)
Harris *et al*, 2016	TNF-α	AVX-470	Active UC	Clinical response: 4 weeks: 25.9%	-	(41)
Hartman *et al*, 2016	TNF-α	AVX-470	Active UC	Decreased TNF, MPO and epithelial cell apoptosis in colon tissue after 4 weeks of treatment	-	(42)
Hibi *et al*, 2017	TNF-α	Golimumab	Moderately to severely active UC	Clinical remission: 54 weeks: 50%	Phase Ⅲ	(43)
Panés *et al*, 2022	TNF-α	Adalimumab	Moderately to severely	Clinical remission:	Phase Ⅲ	(44)

			active UC	8 weeks: 10.9% (standard induction regimen), 13.3% (higher induction regimen) 52 weeks: 29-41.1% (different dosing regimens)		
Rutgeerts *et al*, 2015	TNF-α	Golimumab	Moderately to severely active UC	Clinical remission: 6 weeks: 44% (2 mg/kg), 41.6% (4-mg/kg)	Phase Ⅱ/Ⅲ	(45)
Sandborn *et al*, 2013	TNF-α	HMPL-004	Mildly-to-moderately active UC	Clinical remission: 8 weeks: 34% (1200 mg), 38% (1800 mg)	-	(46)
Sands *et al*, 2019	TNF-α	Adalimumab	Moderately to severely active UC	Clinical remission: 52 weeks: 22.5%	Phase Ⅲb	(47)
Schreiber *et al*, 2021	TNF-α	Infliximab	Active UC	Clinical remission: 54 weeks: 68.4%	Phase Ⅰ	(48)
Suzuki *et al*, 2014	TNF-α	Adalimumab	Moderately to severely active UC	Clinical remission: 8 weeks: 43% (adalimumab 80/40), 50% (adalimumab 160/80) 52 weeks: 23%	Phase Ⅱ/Ⅲ	(49)
Syversen *et al*, 2021	TNF-α	Infliximab	Moderately to severely active UC	Clinical remission: 52 weeks: 19.7%	Phase Ⅲ	(50)

Tajiri *et al*, 2019	TNF-α	Infliximab	Pediatric patients with moderate-to-severe UC	Clinical remission: 30 weeks: 42.9%	Phase Ⅲ	(51)
Tang *et al*, 2011	TNF-α	HMPL-004	Mildly-to-moderately active UC	Clinical remission: 8 weeks: 21%	-	(52)
D'Haens *et al*, 2024	IL-12/23	Mirikizumab	Moderately to severely active UC	Clinical remission: 52 weeks: 36.1%	Phase Ⅲ	(53)
Danese *et al*, 2022	IL-12/23	Ustekinumab	Moderately to severely active UC	Clinical remission: 2 weeks: 20.0% (130 mg), 20.2% (6 mg/kg)	Phase Ⅲ	(54)
Peyrin-Biroulet *et al*, 2023	IL-12/23	Guselkumab	Moderately to severely active UC	Clinical response: 12 weeks: 60.7% (400 mg), 61.4% (200 mg) 24 weeks: 50.0% (400 mg), 54.3% (200 mg)	Phase IIb	(55)
Sands *et al*, 2019	IL-12/23	Ustekinumab	Moderately to severely active UC	Clinical remission: 8 weeks: 15.5% (6 mg/kg), 15.6% (130 mg) 44 weeks: 38.4%,43.8%	Phase Ⅲ	(56)
Danese *et al*, 2022	JAK/STAT	Upadacitinib	Moderately to severely active UC	Clinical remission: 8 weeks: 26% (group 1), 34% (group 2) 52 weeks: 42% (group 1), 52% (group 2)	Phase Ⅲ	(58)

Feagan *et al*, 2021	JAK/STAT	Filgotinib	Moderately to severely active UC	Clinical remission: 10 weeks: 11.5% (study B), 26.1% (study A) 58 weeks: 37.2%	Phase IIb/Ⅲ	(59)
Gros *et al*, 2023	JAK/STAT	Filgotinib	Active UC	Clinical remission: 12 weeks: 71.9% 24 weeks: 76.4%	-	(60)
Sandborn *et al*, 2020	JAK/STAT	Upadacitinib	Moderately to severely active UC	Clinical remission: 8 weeks: 8.5-19.6% (different doses)	Phase IIb	(61)
Sandborn *et al*, 2020	JAK/STAT	Izencitinib	Moderately to severely active UC	Day 28: reduced trend of UC disease activity.	Phase Ⅰb	(62)
Sandborn *et al*, 2022	JAK/STAT	Tofacitinib	Moderately to severely active UC	Clinical response: 8 weeks: 47.8% 12 months: 70.3% Clinical remission: 12 months: 44.6%	Phase II	(63)
Sandborn *et al*, 2017	JAK/STAT	Tofacitinib	Moderately to severely active UC	Clinical remission: 8 weeks: 16.6% (trial 2), 18.5% (trial 1)	Phase Ⅲ	(64)

				52 weeks: 34.3% (5 mg), 40.6% (10 mg)		
Sands *et al*, 2018	JAK/STAT	Peficitinib	Moderately to severely active UC	Clinical remission: 8 weeks: 15.9-27.3% (different doses)	Phase II	(65)
Singh *et al*, 2024	JAK/STAT	Tofacitinib	Moderately active UC	Clinical remission: 8 weeks: 16.28%	-	(66)
Sandborn *et al*, 2012	JAK/STAT	Tofacitinib	Moderately to severely active UC	Clinical remission: 8 weeks: 13-48% (different doses)	Phase II	(67)
Danese *et al*, 2020	PDE4	Apremilast	Active UC	Clinical remission: 12 weeks: 21.8% (40 mg), 31.6% (30 mg) 52 weeks: 32.7% (40 mg), 40.4% (30 mg)	Phase II	(68)
Schreiber *et al*, 2007	PDE4	Tetomilast	Mildly to moderately active	Clinical improvement: 8 weeks: 39% (50 mg), 52% (25 mg)	Phase II	(69)
Danese *et al*, 2024	S1P1	Ozanimod	Moderately to severely active UC	Clinical remission: 52 weeks: 54%	Phase Ⅲ	(70)
Sandbrorn *et al*, 2021	S1P1	Ozanimod	Moderately to severely active UC	Clinical remission: 10 weeks: 18.4% 52 weeks: 37.0%	Phase Ⅲ	(71)

Sandborn *et al*, 2016	S1P1	Ozanimod	Moderately to severely active UC	Clinical response: 8 weeks: 54% (0.5 mg), 57% (1 mg) Clinical remission: 32 weeks: 21% (1 mg), 26% (0.5 mg)	Phase II	(72)
Sandborn *et al*, 2020	S1P1	Etrasimod	Moderately to severely active UC	12 weeks: endoscopic improvement occurred in 41.8% of patients	Phase II	(73)
Sandborn *et al*, 2023	S1P1	Etrasimod	Moderately to severely active UC	Clinical remission: 12 weeks: 25% (group 12), 27% (group 52) 52 weeks: 32%	Phase Ⅲ	(74)

UC, ulcerative colitis; JAK, Janus kinase; PDE4, 3',5'-cyclic-AMP phosphodiesterase 4; S1P1, sphingosine 1-phosphate receptor 1; HMPL-004, andrographolide; MPO, Myeloperoxidase.

Table SII. RAGE inhibitors.

First author, year	Inhibitors	Binding domain to RAGE	Effects	(Ref.)
Hudson and Lippman, 2018	Azeliragon	V	AGEs, HMGB1, S100B and Aβ-RAGE binding inhibition	(84)
Aljohi *et al*, 2018	Momordica charantia	-	AGEs-RAGE binding inhibition	(236)
Watson *et al*, 2012	Alagebrium	-	Reduced AGE accumulation	(237)
Zhang *et al*, 2018	N-benzyl-4-chloro-N-cyclohexylbenzamide	V	AGEs	(238)
Arab *et al*, 2022	Troxerutin	-	HMGB1-RAGE binding inhibition	(239)
He *et al*, 2022	N-benzyl-4-chloro-N-cyclohexylbenzamide	V	HMGB1-RAGE binding inhibition	(240)

Tang *et al*, 2022	Tanshinone IIA	-	HMGB1	(241)
Shihui *et al*, 2024	N-benzyl-4-chloro-N-cyclohexylbenzamide	V	S100	(242)
Ding *et al*, 2020	Tanshinone IIA	-	Aβ-RAGE binding inhibition	(243)
Liu *et al*, 2023	Tanshinone IIA	-	Matrix metalloproteinase-9	(244)

S100, protein S100; AGEs, advanced glycation end products; RAGE, receptor for AGEs; Aβ, amyloid β; HMGB1, high-mobility group box 1.