

Investigational Therapies for HCU

Concept	Program	2021	2022	2023	2024	2025	2026	2027		
Systemic Enzyme Therapies to degrade HCY	TVT-058 PEG-CBS Enz Replacement Therapy (Travere)	Phase I/II	D A	RR	Phase III	D A	F	Reg Review	Market Launches	
	AGLE-177R Engineered homocystinase (Aeglea)	POC IND	Phase I/II	DA	RR	Phase III	DA	F	Reg Review	ML
Oral (GI) Enzyme Therapies to prevent MET absorption	CDX-6512 Methionine-Gamma-Lyase (Codexis)	Preclinical POC	Timelines unknown – estimated 5-7 years from IND filing/Phase I to market launches							
	SYNB1353 Eng probiotic metabolizes MET (Synlogic)	Preclinical POC; IND	R R	Ph I	DA	RR	Phase II	D A	RR	Phase III
Gene Therapy	AAV-CBS Gene transfer (Kruger/Crystal)	Preclinical POC	Timelines unknown – estimated 5-7 years from IND filing/Phase I to market launches							
Metabolic Pathway Modification	Formate combined with Betaine (Ken Maclean)	Preclin POC	Timelines unknown – estimated 5-7 years from IND filing/Phase I to market launches							
	Increase Hcy bioavail via thiol-based reductants – syn with ERT (T Majtan)	Preclin POC	Timelines unknown – estimated 5-7 years from IND filing/Phase I to market launches							

Legend: POC – Proof of Concept; IND – Investigational New Drug Application; DA – Data Analysis; F – Filing with Regulatory Agencies; R – Regulatory Review; ML – Market Launches