

Investigational Therapies for HCU

RESEARCH MAP

Expected Development Time-Lines Informed by General Industry Assumptions. These time-lines have not been confirmed by the program sponsors.

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	RR	ML		
	AGLE-177R Engineered homocystinase (Aeglea)	POC IND	Phase I/II	D A	RR	Phase III	D A	F	RR	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	RR	Phase I	D A	RR	Phase II	D A	RR	Phase III	F
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)	Preclinical 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)	Preclinical 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; RR - Regulatory Review; ML - Market Launches