

Another phenylketonuria hold, courtesy of Homology



Madeleine Armstrong

The phenylketonuria pipeline already had one project on clinical hold, and now it has another: Homology Medicines' HMI-102 on Friday joined Biomarin's BMN 307 in attracting scrutiny from the FDA. It is not yet clear exactly what the problem is with HMI-102, but Homology cited "elevated liver function tests" in the phase 1/2 Phenix trial. Stifel analysts suggested that Homology might have seen abnormally high or non-transient liver enzyme elevations, or that steroids could have failed to lower these enzymes. The news came a day after Biomarin said the [clinical hold of BMN 307](#) would drag on a while longer: the FDA has requested more preclinical data, which is expected to take several quarters. That group needs to assuage concerns about cancer risks with its project after tumours were seen in mouse studies. Since *Evaluate Vantage* last looked at the PKU pipeline PTC Therapeutics' PTC923 has moved into phase 3. This has a similar mechanism to Biomarin's approved therapy Kuvan, which is only suitable for a fraction of patients; still, [PTC says PTC923 could be used in a broader population](#). Homology, which fell 37% after hours, also recently took a gene editing asset, HMI-103, into the clinic.

The clinical-stage phenylketonuria pipeline

Project	Company	Description	Trial details
Phase 3			
PTC923	PTC Therapeutics	Synthetic prodrug of tetrahydrobiopterin (BH4)	Data from Aphenity due YE 2022
Phase 2			
SYNB1618	Synlogic	Engineered <i>E coli</i> strain (consumes Phe)	Ph2 Synpheny-1 final data due H1 2022, most promising strain to progress to ph3
SYNB1934	Synlogic	Engineered <i>E coli</i> strain (consumes Phe)	Ph2 Synpheny-1 final data due H1 2022, most promising strain to progress to ph3
HMI-102	Homology Medicines	PAH gene therapy (AAVHSC vector)	Ph1/2 Phenix on clinical hold; data had been due mid-2022
BMN 307	Biomarin Pharmaceutical	PAH gene therapy (AAV5 vector)	Ph1/2 Phearless on clinical hold after preclinical findings; new preclinical data request to take "several quarters"
Phase 1			
HMI-103	Homology Medicines	In vivo PAH gene editing (AAVHSC vector)	Phedit not yet recruiting
CDX-6114	Codexis/Nestlé	PAL-like enzyme	Ph1 completed, ph1b planned in 2022

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