

Arrowhead shoots after hypoxia



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[Merck & Co's \\$1.05bn takeover of Peloton Therapeutics](#) last year focused on a new mechanism targeting tumour hypoxia, and now Arrowhead has got in on the game by starting a phase Ib study. Arrowhead's ARO-HIF2 is an RNAi project that targets the transcription factor HIF-2 α , which is involved in regulating the body's response to low oxygen, now being tested in renal cell carcinoma. Peloton's PT2977, now called MK-6482, was the first project to hit HIF-2 α , and Merck paid up handsomely. MK-6482 has oral administration advantages, as ARO-HIF2 will be given by intravenous infusion, and Merck's project has shown promising early data; a phase III study is under way, also in kidney cancer, versus Afinitor. Checkpoint inhibitors are becoming dominant in renal cancer, and combination strategies could move HIF-2 α inhibitors into earlier lines of therapy.

Targeting HIF-2 α , the clinical trials so far

Project	Company	Clinical trial	Details	Data?
MK-6482 (PT2977)	Merck & Co (ex Peloton)	MK-6482-005	Phase III, vs Afinitor, n=736	Primary completion 2025
		NCT03401788	Ph II in von Hippel -Lindau disease-associated renal cell cancer, n=61	28% ORR
		NCT03634540	Ph II Cabometyx combo, n=188	Primary completion 2023
		NCT02974738	Ph I, n=125	Early data in 55 patients showed 24% ORR
ARO-HIF2	Arrowhead	AROHIF21001	Phase Ib dose-finding study in up to 18 patients	Primary completion 2022

Sources: EvaluatePharma, clinicaltrials.gov, company releases.