September 17, 2020

Arrowhead gets a $1.4bn boost from flattering data

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Arrowhead previously played down hopes for its rare liver disease candidate ARO-AAT, so investors were pleasantly surprised by the limited data released yesterday. But it is hard to see why the group added $1.4bn in market cap on results that theoretically might have come from one patient. Arrowhead claimed to be reporting interim six-month liver biopsy data from four subjects in a phase II open-label study of ARO-AAT. The project is being developed for alpha-1 antitrypsin deficiency (AATD), a genetic disorder characterised by the build-up of mutant AAT protein (Z-AAT) in the liver. However, rather than reporting average values, Arrowhead only gave the best reported patient outcome for most endpoints – so, for example, serum and total intra-hepatic Z-AAT decreased by a maximum of 93% and 95% respectively. The group also reported a maximum 97% reduction in Z-AAT polymer – this was considered encouraging, since investors had previously been told that it might be too early to see a benefit here. This is no doubt what caused the excitement yesterday, but much more complete data are needed to draw reliable conclusions. Arrowhead hopes to present results from all four patients at the AASLD meeting in November; the pivotal Sequoia trial is ongoing.

Selected AATD projects in development

Project	Company	Description	Status	Note
ARO-AAT	Arrowhead Pharmaceuticals	RNAi therapeutic	Phase II/III, NCT03946449 & NCT03945292	Interim data reported
VX-814	Vertex Pharmaceuticals	Alpha-1 proteinase inhibitor	Phase II, NCT04167345	Data due YE 2020/Q1 2021
VX-864	Vertex Pharmaceuticals	Alpha-1 proteinase inhibitor	Phase II, NCT04474197	Trial began Jul 2020
DCR-A1AT	Dicerna Pharmaceuticals	RNAi therapeutic	Phase I/II, NCT04174118	Dicerna & Alnylam co-developing
ALN-AAT02	Alnylam Pharmaceuticals	RNAi therapeutic	Phase I/II, NCT03767829	Dicerna & Alnylam co-developing

Source: EvaluatePharma, clinicaltrials.gov.