Evaluate Vantage

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Negative dose response clouds Insmed’s day of glory

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With results of INS1007’s Willow study in non-cystic fibrosis bronchiectasis under its belt Insmed put on 41% yesterday, its $2.6bn valuation reflecting the fact that it might no longer be reliant solely on the marketed antibiotic Arikayce. However, close reading of the data throws up a red flag: only the lower of two INS1007 doses was efficacious, something that hints at the finding being due to luck. Willow’s primary endpoint, time to first pulmonary exacerbation at 24 weeks, was just about met by both the 10mg and 25mg doses, though Insmed does not reveal whether the analysis was sequential and whether some subjects were excluded. But rate of pulmonary exacerbations, a secondary measure, was at least as important since this will likely be the primary endpoint of a pivotal trial, and here only 10mg yielded a p value below 0.05. Nevertheless, even though 25mg was not significant, its reduction versus placebo beat a previously defined 20% threshold for proceeding to phase III; moreover, Willow did not show the epidermal desquamation toxicity that had derailed a similar Glaxosmithkline project. Stifel analysts put the lack of dose response down to patient heterogeneity, and said INS1007 could generate blockbuster sales by 2029.

Summary of Insmed's Willow trial (n=256)			
	INS1007 10mg once daily	**INS1007 25mg once daily**	**Placebo**
Time to first pulmonary exacerbation vs placebo (24wk)*	Not disclosed	Not disclosed	NA
p value	0.027	0.044	NA
Rate of pulmonary exacerbations vs placebo (24wk)	36%	25%	NA
p value	0.041	0.167	NA
Rate of adverse events leading to discontinuation	10.6%	7.4%	6.70%
*Source: company press release; *primary endpoint.*			