Vertex (VRTX) '661/Kalydeco Fails Interim In Het/Min; Expectations Were Low

Key Takeaway

VRTX announced that '661/Kalydeco missed on its interim efficacy analysis in het/min CF pts; while success would have created an opportunity to reach this large subpopulation with the dual combo and at least reaffirmed '661's activity (given its importance as a backbone for the triple), we believe expectations were low, and this does not change our overall positive CF franchise view.

Though would have been an upside catalyst, not a major surprise that a dual combo - '661/Kalydeco - was insufficient in the het/min population. We believe there was modest hope that this combo might fare better than Orkambi in this difficult-to-treat het/min population, given potential for improved activity attributes for the '661 component relative to lumacaftor (better lung penetration, favorable FEV-1 improvements in other F508del populations, benefits in G551D/gating when added to Kalydeco). A positive interim, while not necessarily guaranteeing success of the overall phase III, would have created the potential for Vertex to reach this population with less dependence on the early-stage next-gen correctors and would have helped reaffirm '661's activity as an optimal backbone for the triple combo. However, given the prior failure of Orkambi in this setting and the much better preclinical data for a triple combo in this population, we believe most assumed '661/Kalydeco in het/mins had a low likelihood of working and that a 3x combo would be needed in this population. The impact to our valuation on eliminating the low probability NT sales ests. for 661/Kalydeco in het/mins would be $2 but we continue to see a 70% probability VRTX ultimately succeeds in this population with a triple combo.

Few details in PR or from company discussions make it difficult to have any increased clarity on '661's ultimate likelihood of success in other populations, though timelines for those other ph.IIIs appear intact. VRTX is still not disclosing the bar for this interim analysis, so it is difficult to know if any small signals activity were observed, though we believe if there were any lung function benefits worth following up on the study would likely have proceeded to part 2. Presentation of the full data is unlikely to be at NACF this year, meaning it will be more likely presented with data from other ph.IIIs next year-- so unlikely to have any insights into the data details before the other ph.III '661 readouts. Encouragingly, safety continues to look good for '661 (DSMB indicated to VRTX no safety signals were seen, though no specifics on bronchoconstriction), and we continue to believe the combo will provide an improved benefit/risk profile vs Orkambi given lower cough/chest tightness seen in other studies. Encouragingly, timelines for the other three '661/Kalydeco studies remain on track: Completion of enrollment in September of the ph.III trial in residual function patients with data in 1H17 is in-line with company guidance. Guidance for completion of the ph.III study in gating mutation patients and NDA submission remains the same. Next-gen correctors remain on track for combo testing in pts later this year pending ph.I data.
Company Description

Vertex Pharmaceuticals discovers, develops, manufactures, and commercializes small molecule therapeutics, with a core developmental and commercial focus on cystic fibrosis. Marketed products in the CF space include Kalydeco and Orkambi, and earlier-stage programs include fields such as oncology and neurology. Vertex is headquartered in Boston, MA.

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