CD73 Inhibition with a Novel Orally Bioavailable Small Molecule Blocks Adenosine Production and Rescues T-cell Activation

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CD73 mediates immunosuppression and therapeutic resistance via adenosine production

1. ORIC’s novel CD73 inhibitors potently suppress adenosine production from AMP

2. ORIC-533 and OP-5558 exhibit slow dissociation rate and sustained effects after washout

3. ORIC-533 rescues activation of CD8+ T-cells exposed to AMP

4. ORIC’s potent AMP-competitive inhibitors are active in a high AMP environment

5. CD73 inhibition efficiently restores AMP-induced transcriptional changes

CONCLUSIONS

ORIC-533 is a novel CD73 inhibitor with best-in-class properties

• Potently blocks adenosine production from AMP
• Has slow dissociation rate / long residency time on CD73 protein
• Continues to inhibit adenosine production after drug washout
• Rescues activation of CD6+ T-cells exposed to AMP
• Potent in high AMP [1mM] environment

See also: AACR 2020 Poster #10268 An Orally Bioavailable Inhibitor of CD73 Reverts Intratumoral Immunosuppression and Promotes Anti-tumor Response

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