An Orally Bioavailable Inhibitor of CD73 Reverts Intratumoral Immunosuppression and Promotes Anti-Tumor Response

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**BACKGROUND**

CD73 (ecto-5'-nucleotidase):

- Is required for adenosine (ADO) production and linked to therapy resistance.
- Is overexpressed across cancer types driving local elevation of ADO.
- Overexpression is correlated with poor prognosis.
- Mediates immunosuppression and chemoresistance via ADO production.

1. ADO signaling is broadly immunosuppressive

2. Discovery of potent and orally bioavailable CD73 inhibitors

3. ORIC CD73 inhibitors rescue AMP-mediated CD8+ T cell suppression

4. Oral dosing of OP-5558 and ORIC-533 significantly inhibit tumor growth and reduce intratumoral ADO

5. ORIC CD73 inhibitors relieve intratumoral immune suppression

**CONCLUSIONS**

ORIC’s orally bioavailable small molecule CD73 inhibitors:

- Potently suppress ADO production in vitro.
- Restore cytokine secretion of ADO-suppressed CD8+ T cells.
- Significantly reduce adenosine levels in tumors in vivo.
- Achieve significant tumor growth inhibition as single agents with oral delivery.
- Demonstrate in vivo immune modulation consistent with decreased immunosuppression.

See also: AACR 2020 Poster #4317 CD73 inhibition with a novel orally bioavailable small molecule blocks adenosine production and rescues T cell activation.

Thank you to the ORIC CD73 team!