

Preparation of a clinical trial with α -TIGIT antagonist antibody EOS-448, which demonstrates potent preclinical activity and safe toxicology profile

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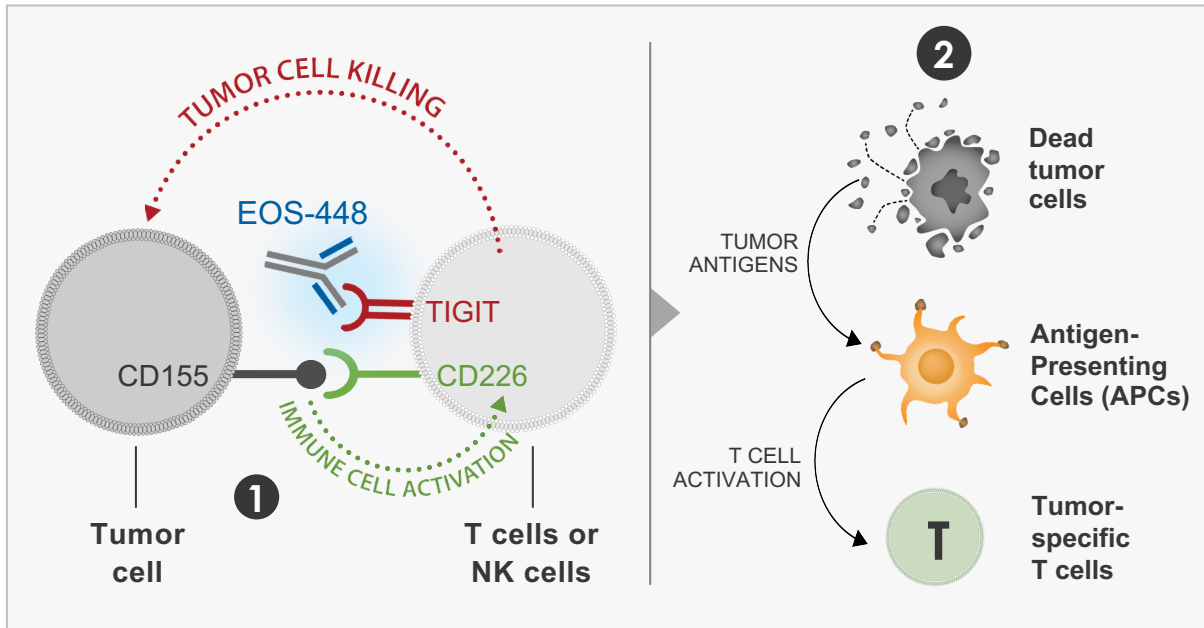
Author Disclosure Information

- All authors are (or were former) employee of iTeos Therapeutics SA

Multiple Mechanisms of Action of EOS-448 to Restore Antitumor Immunity

MECHANISM 1:

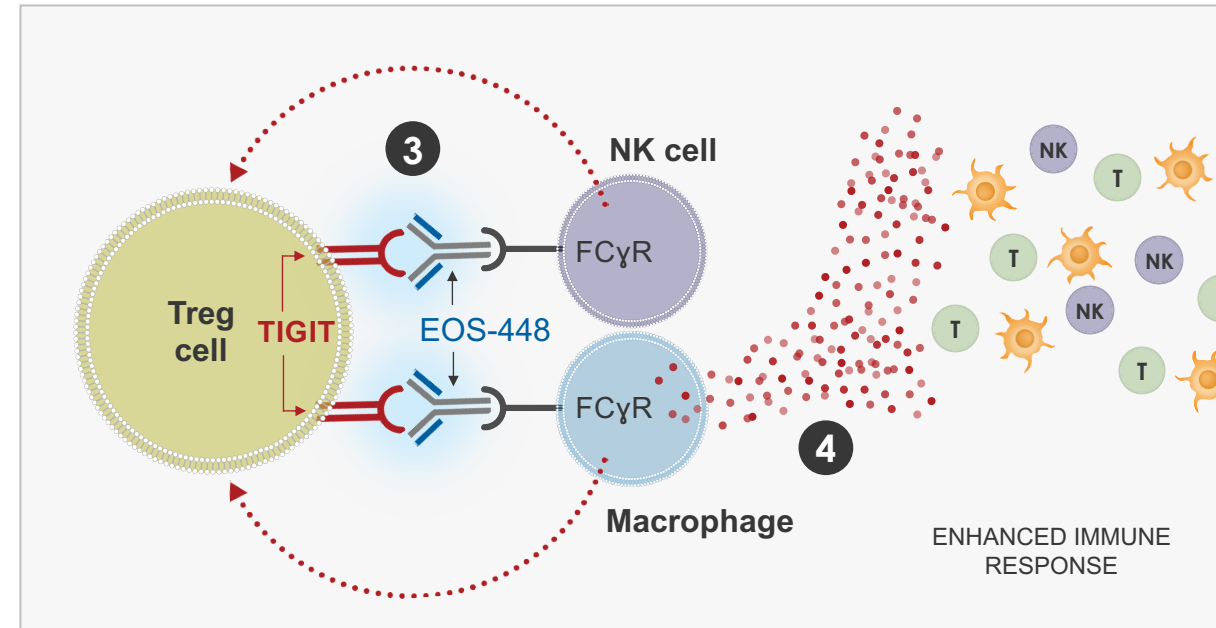
EOS-448 blocks the TIGIT receptor, enhancing anti-tumor activity, and the death of tumor cells further augments the immune response.



- 1 EOS-448 blocks TIGIT, increasing the availability of CD155/CD112 to bind to CD226 receptor, without competition. This blocks the activation of TIGIT's immunosuppressive function and activates anti-tumor immune cells.
- 2 Tumor destruction can lead to cross presentation of antigens by Antigen Presenting Cells (APCs) to T cells and augmentation of the immune response.

MECHANISM 2:

EOS-448 depletes immunosuppressive Treg cells, and EOS-448 stimulates cytokines to activate more immune cells.

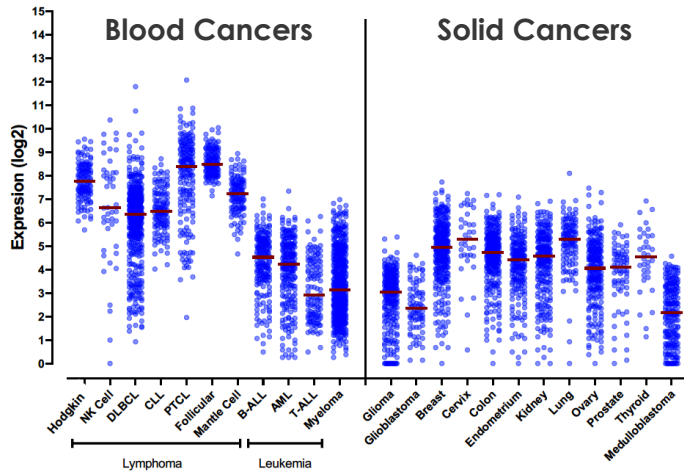


- 3 Regulatory T cells (Tregs) inhibit the anti-tumor function of cytotoxic T cells. EOS-448 binds to TIGIT which is highly expressed on the surface of Tregs and stimulates NK cells and macrophages mediated cytotoxicity via FcγR engagement.
- 4 NK and macrophage activation stimulates the release inflammatory cytokines that signal and activate other immune cells to further augment the anti-tumor response.

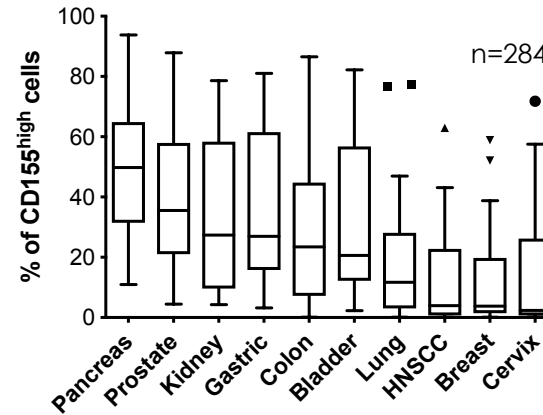
EOS-448 has a Competitive Profile with Potential for Benefit in a Broad Range of Cancer Indications

Members of TIGIT pathway are highly expressed in many cancer indications

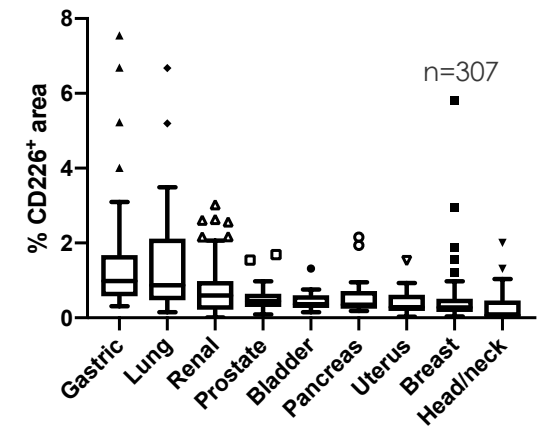
Expression of TIGIT mRNA in solid and heme cancers



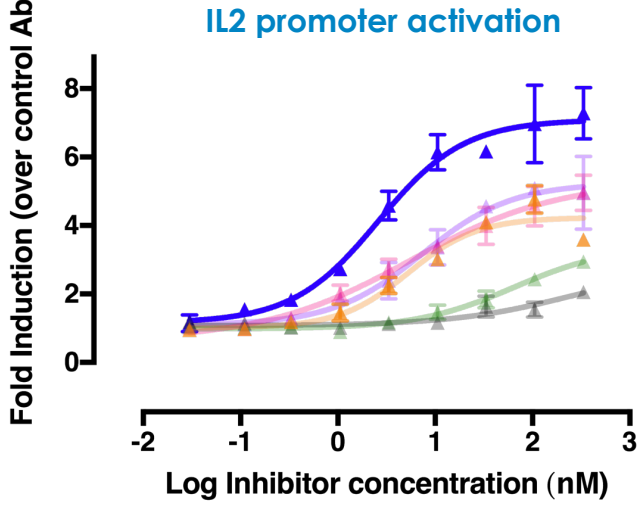
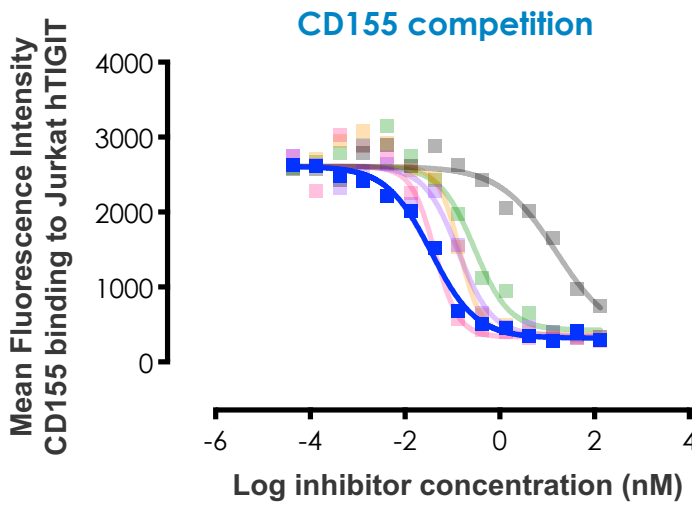
CD155 protein is highly expressed in solid tumors



CD226 protein is expressed on immune-infiltrating cells



Immunomodulatory activity of EOS-448: Potent competitive profile

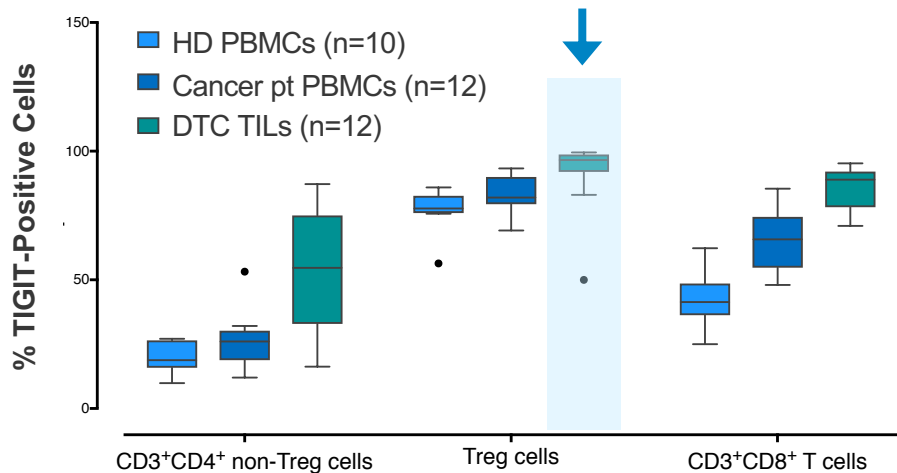


- EOS-448
 - Mereo
 - Genentech
 - BMS
 - Merck
 - Arcus
- Sequences from :
- Mereo = 313M32 from US2016/0376365 A1
 - Genentech = 4.1D3 from WO2017/053748 A2
 - BMS = 22G2 from US2016/0176963 A1
 - Merck = Clone 31C6 from WO2016/028656vA1
 - Arcus = TIG1 from WO2017/152088 A1

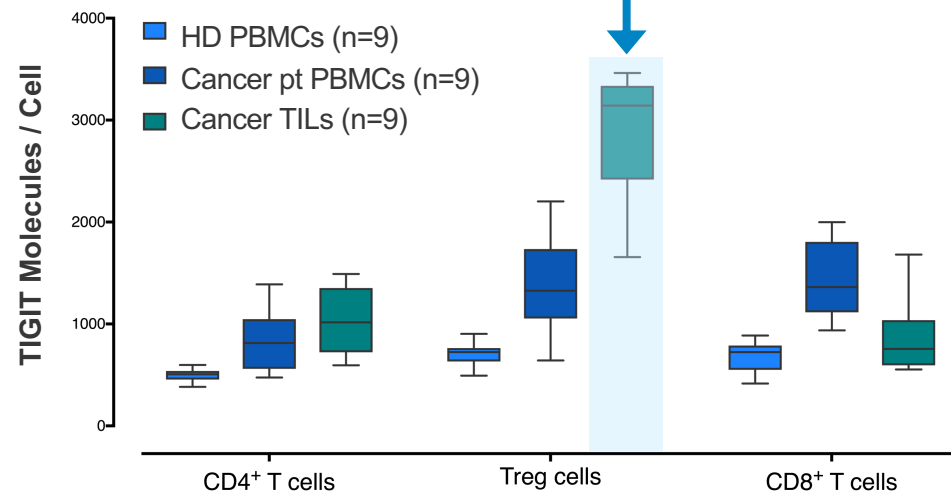
Tregs, Particularly TILs, Express the Highest Level of TIGIT, Making Tregs a Preferred Target for Depletion by EOS-448

TIGIT is expressed in high proportion of circulating CD8+ & Treg cells in cancer patients, with highest density on Tregs TILs

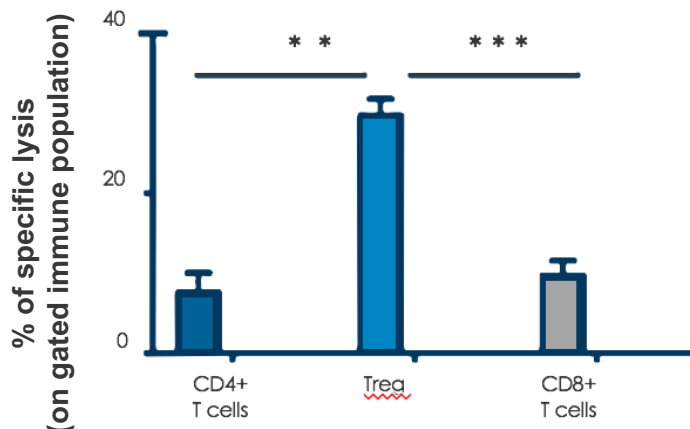
Increased frequency of TIGIT+ T cells in cancer patients



Highest number of TIGIT molecules on Treg from TME

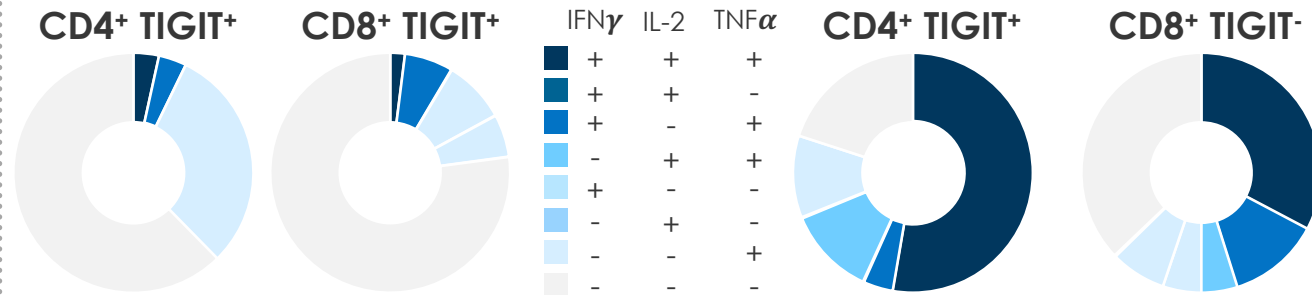


Preferred Treg cytotoxicity of EOS-448



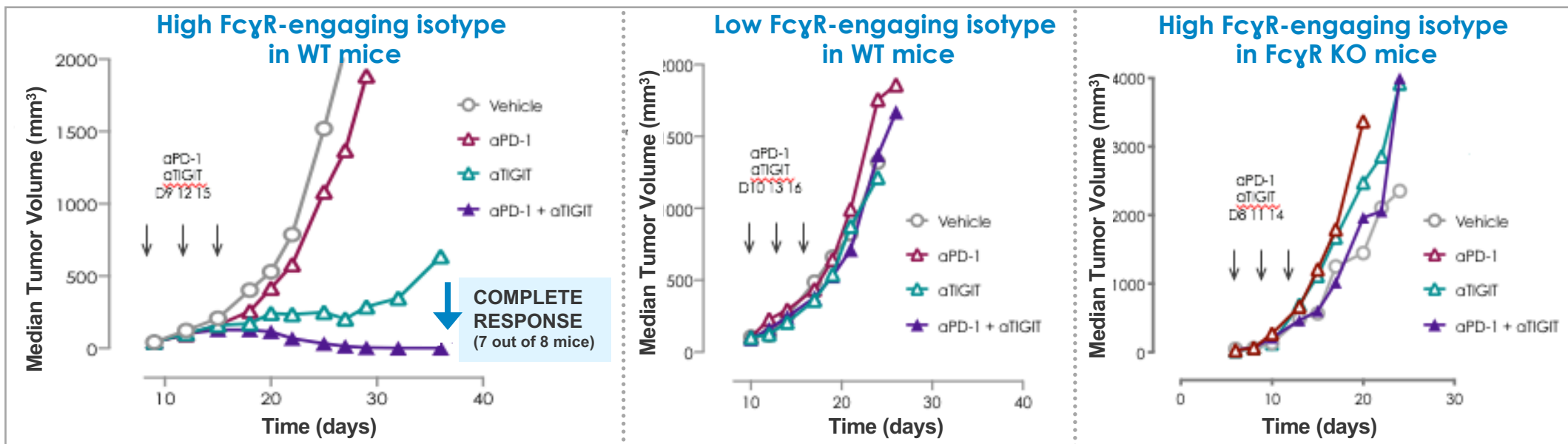
EOS-448 shows preferred cytotoxicity on Tregs and TIGIT+ TILs are dysfunctional

TIGIT-expressing TILs are dysfunctional



FcγR Engagement is *Critical* for Anti-Tumor Activity of α-TIGIT Ab in CT26 Colon Cancer Model

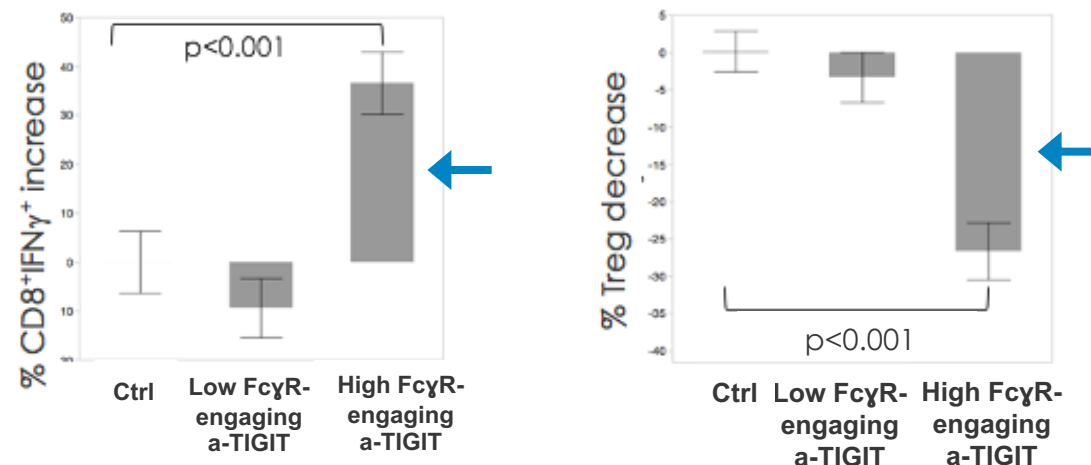
EOS-448 demonstrates strong antitumor activity as single agent & in combination with anti-PD-1 Ab, that is fully dependent on FcγR engagement



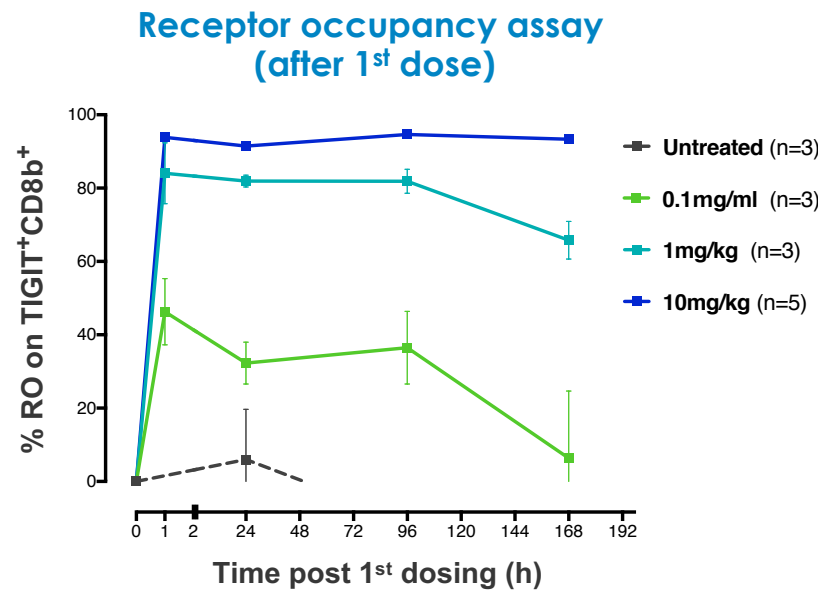
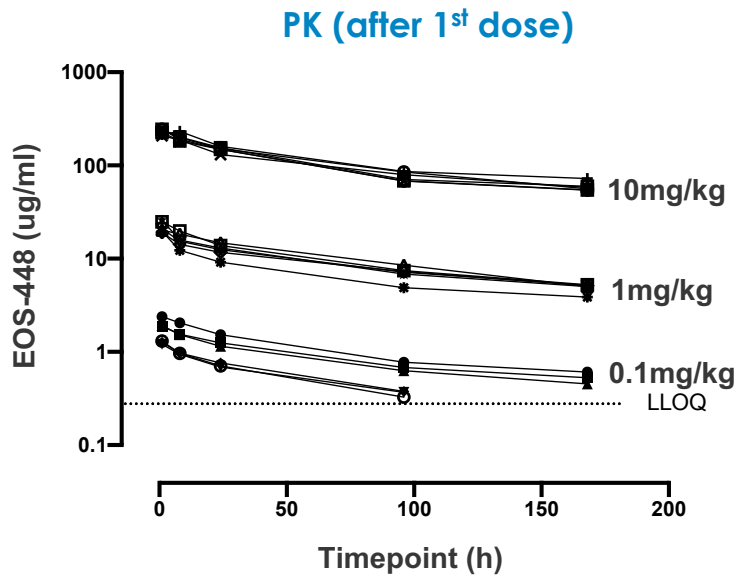
EOS-448 efficacy correlates with increased proportion of IFNγ⁺ TILs and Treg depletion in the TME

Antitumor activity correlates with:

- increased in IFNγ⁺ CD4⁺ and CD8⁺ T cells within TME
- decreased proportion of Treg within TME
- Long-term memory response



Cyno GLP Tox Shows Classical hlgG1 PK Profile for **EOS-448** and Clean Safety Profile with NOAEL* at Highest Tested Dose (10mg/kg)



Clean GLP toxicity profile in cynomolgus

- ✓ Well tolerated at all tested doses
- ✓ No abnormalities during dosing phase and recovery examinations
- ✓ Classical IgG1 PK profile → NOAEL* = HNSTD° = 10mg/kg

*NOAEL = No Observed Adverse Effect Level

°HNSTD = highest non severely toxic dose

Ongoing Phase 1/2 Trial & ongoing preparation of Phase 2 expansions

Single Agent Dose Escalation to Define RP2D

Advanced solid tumor patients (n=30) (NCT04335253):

- Multicenter, open label
- Flat dose infusion
- Mandatory pre- & on-treatment biopsy

Presenter: G. Driessens

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