OncoResponse

Interrogating for **Cures**™

41st Annual J.P. Morgan Healthcare Conference
January 12, 2023

Summary highlights

- **OR2805 (CD163) in clinic**
  - Advancing expansion cohorts in US and Europe
- **OR502 (LILRB2) nearing IND**
  - Clinically validated TME target
- **Proven B-cell platform leveraging Elite Responder data**
  - Rapidly identify fully human therapeutic mAbs and high value targets
- **Broad strategic alliance with MD Anderson Cancer Center**
  - Unique access to Elite Responders and oncology expertise
- **Management team with extensive experience, both private and public**
  - Scientific, clinical, financial & strategic leaders with proven track records
- **High-quality syndicate of strategic and institutional investors**

Proven leadership team

Clifford Stocks

CEO

- 30-year biotech executive with $1B+ in raised capital
- Executive Team that oversaw the commercial success of **Cialis®**
- Key architect of Lilly ICOS JV leading to $2.3B merger in 2007
- Led M&A of Calistoga with Gilead for $600M in 2011 for **Zydelig™**
- MBA, University of Chicago

Bob Lechleider, MD

CMO

- Approval of **Padcev™** for previously treated metastatic urothelial cancer
- Former faculty at Georgetown University Medical School
- Clinical training at Beth Israel-Deaconess and in medical oncology at the NCI
- HHMI Scholar and Damon Runyon postdoctoral fellow

Kamal Puri, PhD

CSO

- Oversaw preclinical research and portfolio strategy
- Advanced discovery candidates into clinical development including **Zydelig™**
- Immunology training in Timothy Springer's Lab at Harvard
- Research Fellow at the Council of Scientific and Industrial Research, India

Chris Russell

CFO

- Executive team that grew Oracle to $200+ billion mkt cap; launched online division
- Helped launch and grow ArcSight (IPO), WageWorks (IPO) and TrustArc
- Strategy consultant at Booz-Allen
- Auditor and former CPA at EY and PwC
- MBA, University of Chicago

Savvy financial backers and strategic relationships

- Strong syndicate of Investors, Board Members and Scientific Advisors
- Broad strategic relationship with MDACC for Elite Responder samples
- $123 million raised; Cash runway into 2024; Series D planned for Q2 2023

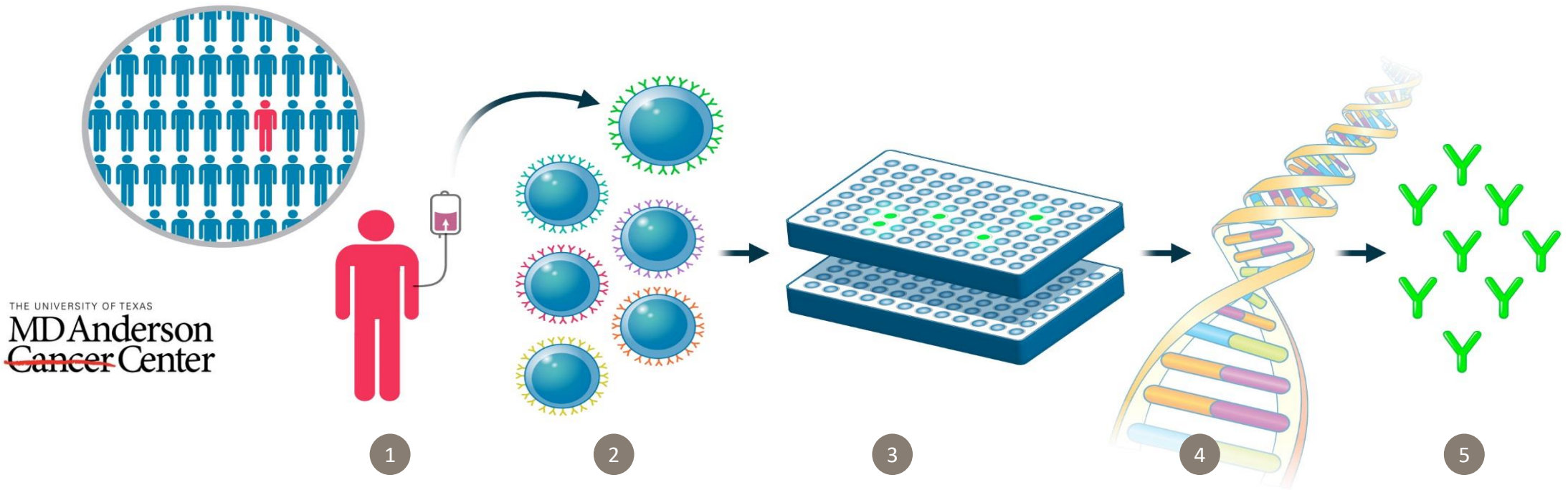
OncoResponse

Our Mission

Attack cancer by harnessing clues from the immune systems of Elite Cancer Responders to disrupt immunosuppression in the tumor microenvironment

OncoResponse platform interrogates the entire B-cell repertoire

Access to Elite Responders → Identify rare Abs inaccessible to other Ab discovery platforms → Develop therapeutic mAb candidates



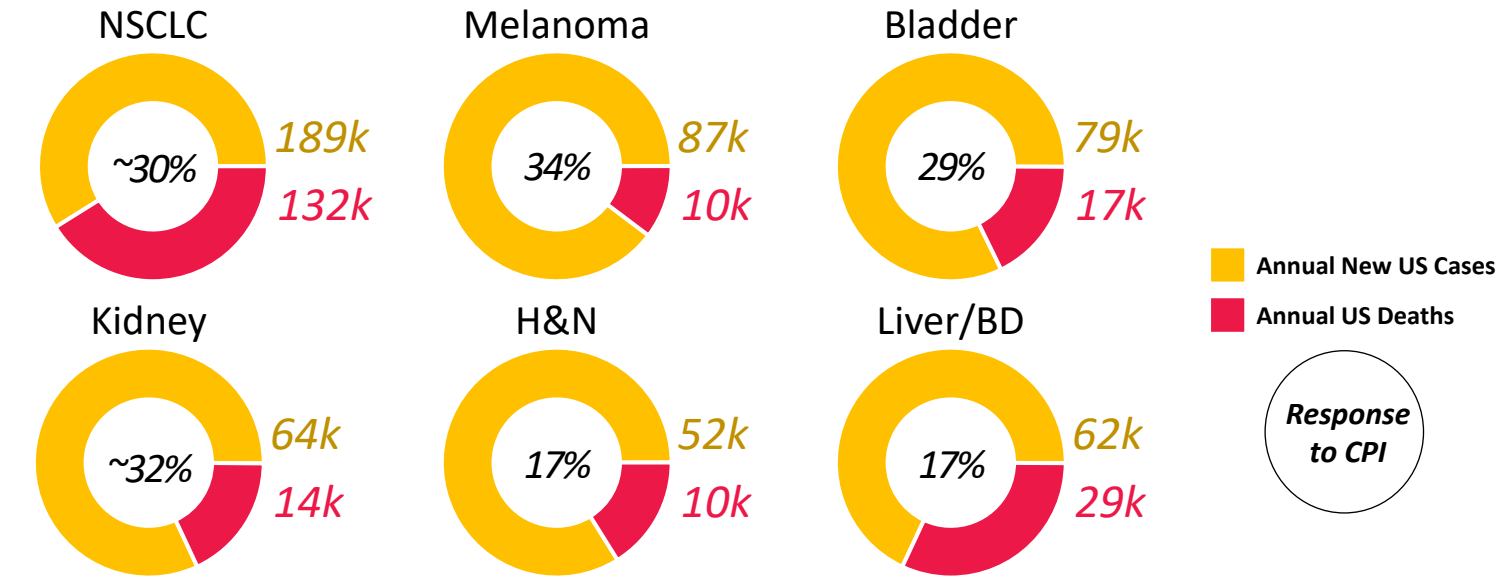
THE UNIVERSITY OF TEXAS MD Anderson Cancer Center

1. Blood/PBMC collection
2. IgG/A^{+} memory B cell activation
3. Rapid functional screening identifies clones with desired properties
4. Deep sequencing of positive clones
5. Recombinant antibodies

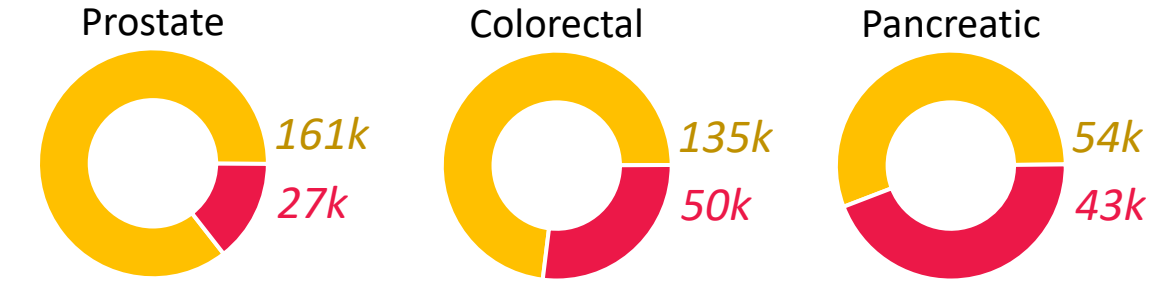
Validated antibody platform for new drug discovery

The Immuno-Oncology (IO) opportunity

CPI-Responsive Cancer Types



CPI-Non-Responsive Cancer Types



Abbreviations: CPI, checkpoint inhibitor; IO, immuno-oncology; TME, tumor microenvironment

- Response to checkpoint inhibitors (CPI) continue to be low due in part to the suppressive Tumor Microenvironment (TME)
- Large unmet need to overcome immunosuppression of the TME to increase response and survival
- **OncoResponse: Discovering new therapies that leverage the immune system to attack cancer**
  - **Rare antibodies from Elite Responders that modulate immunosuppression in the TME**
  - **Used as single agent or in combination with CPI to improve patient outcomes**

OncoResponse

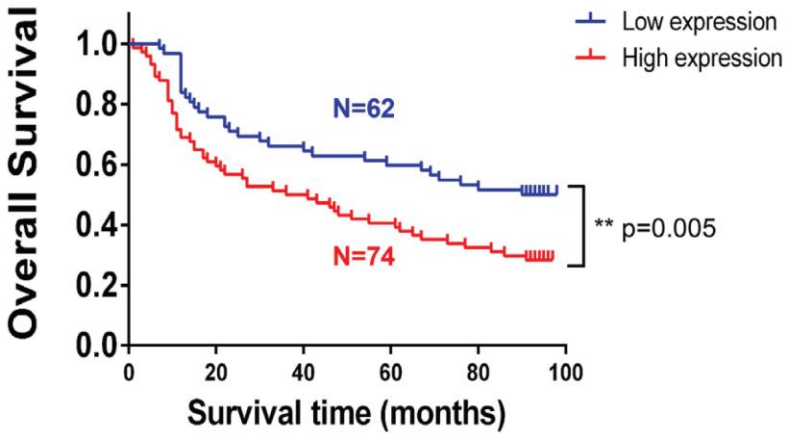
OR2805
anti-CD163 human-derived mAb

Targeting M2 macrophages to reverse immunosuppression of the tumor microenvironment

CD163 is a negative prognostic marker in cancer

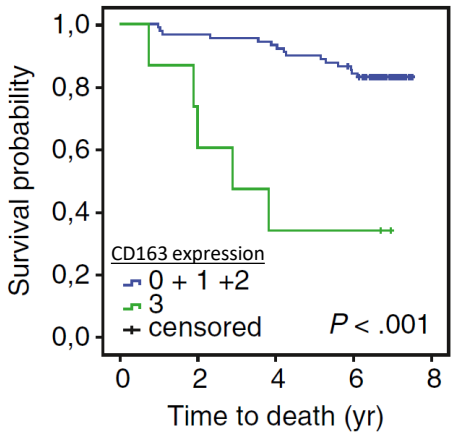
Gastric Cancer[12]

Overall survival



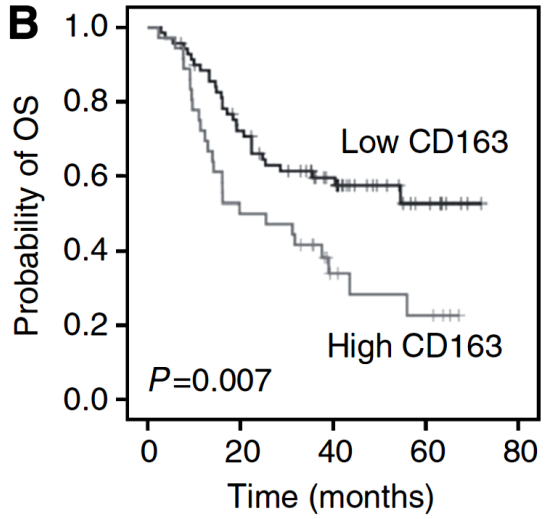
Breast Cancer[13]

Survival probability

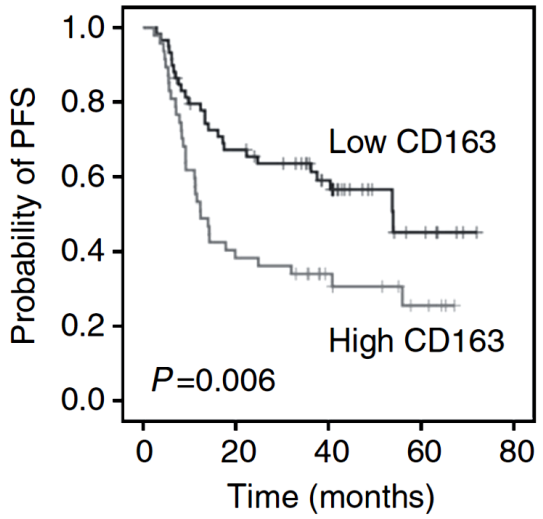


Head and Neck Cancer[14]

Overall survival

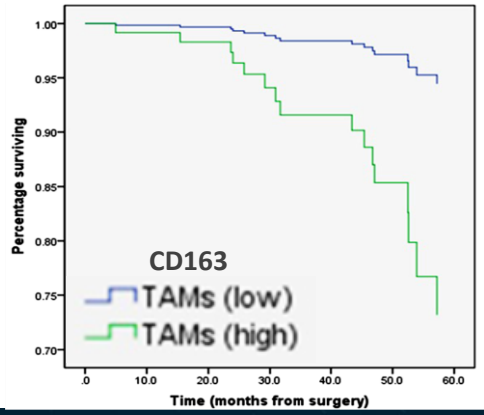


Progression-free survival

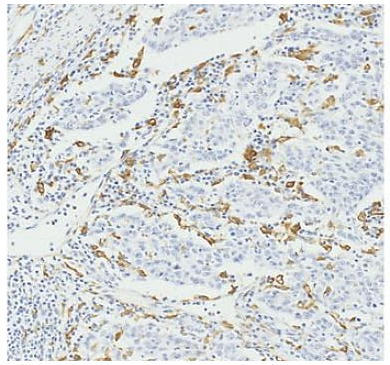


Colorectal Cancer[16]

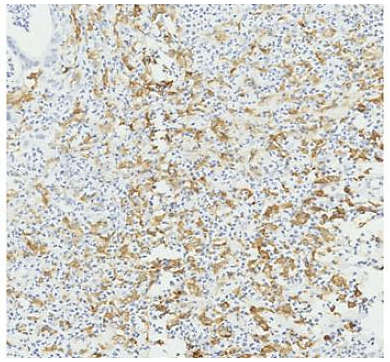
Overall Survival



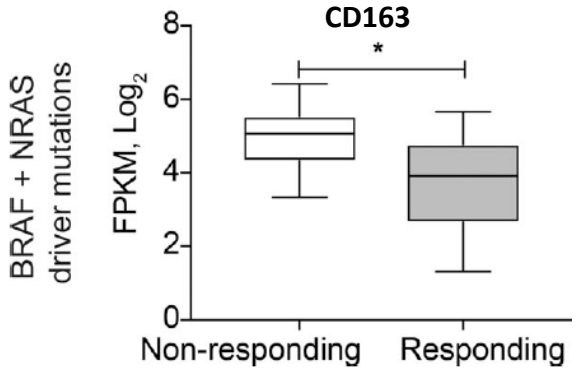
Low TAM Infiltration

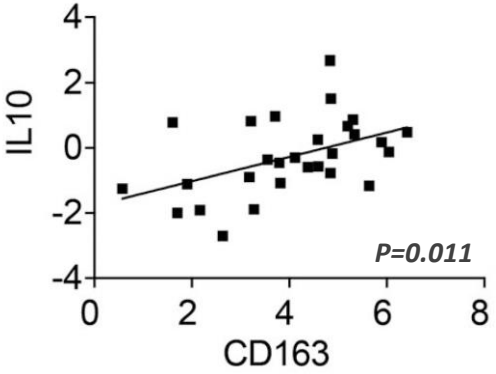


High TAM Infiltration

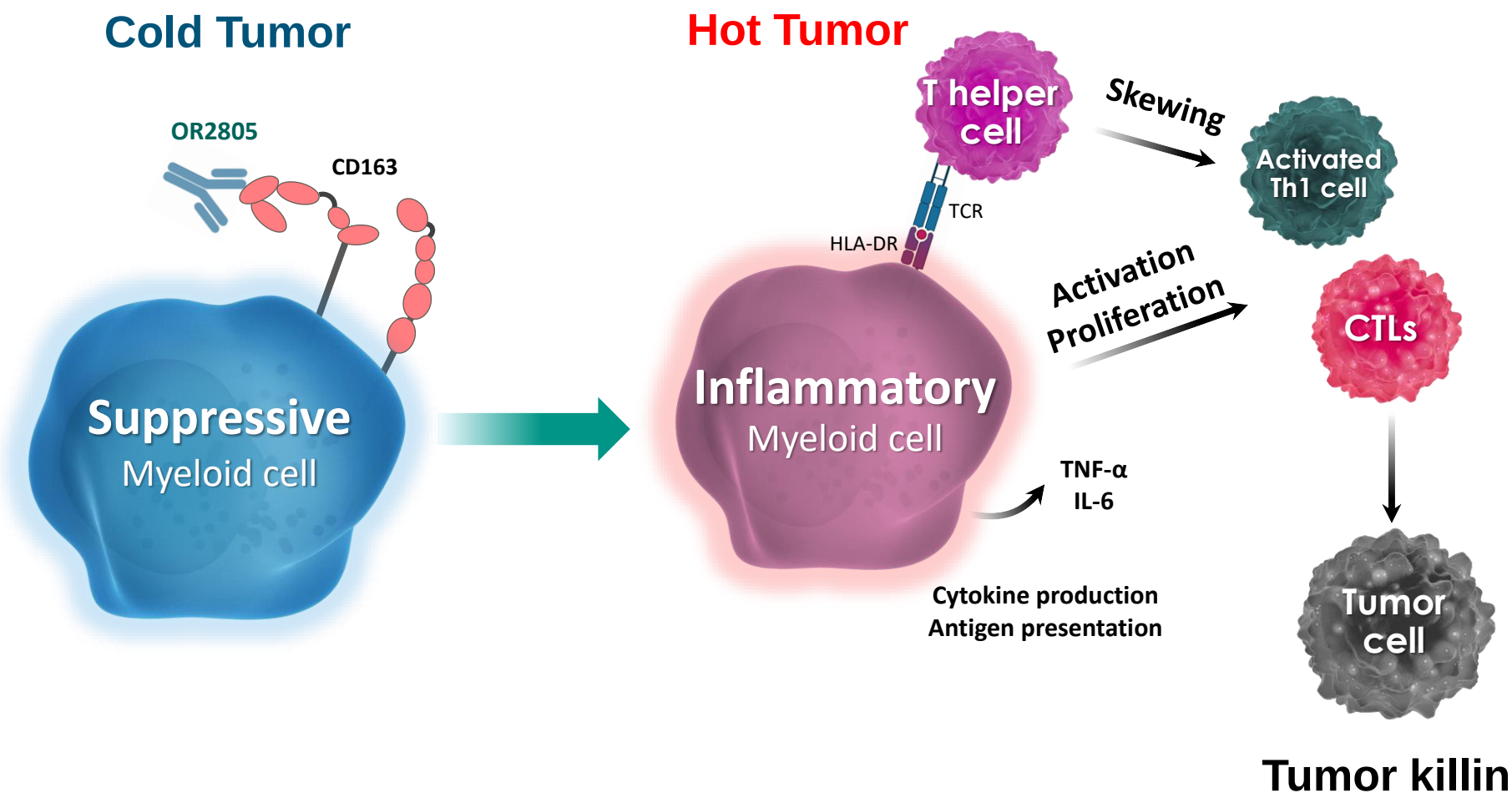


Melanoma patients on anti-PD-1 therapy[15,38]

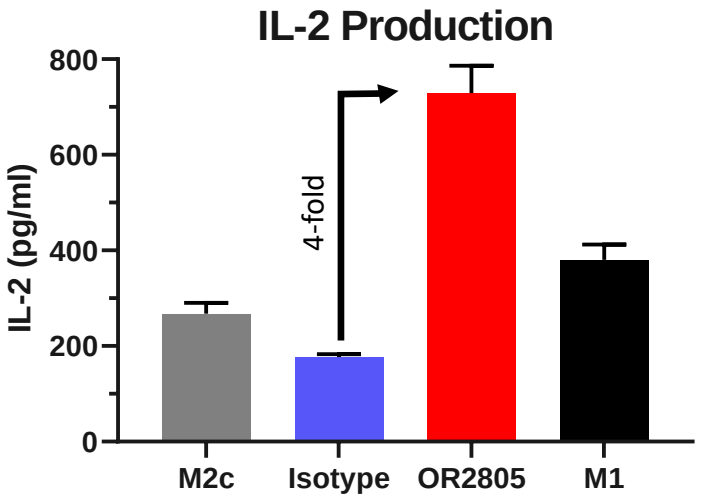




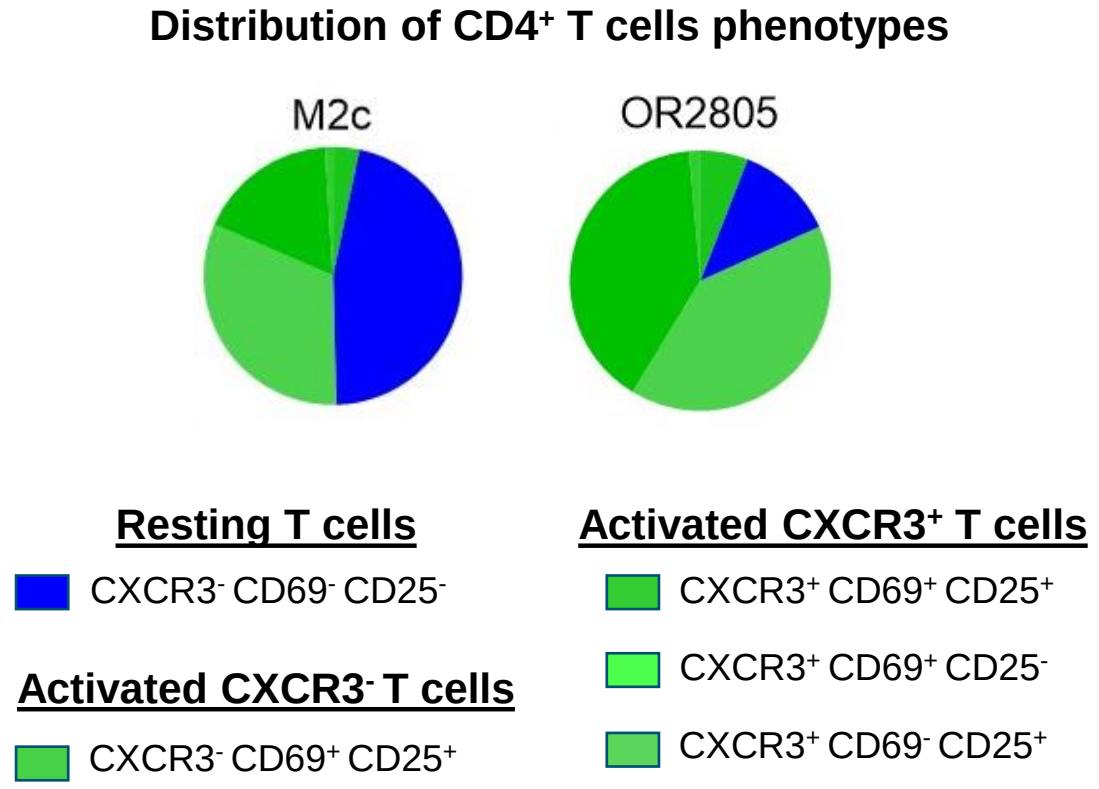
OR2805 relieves immunosuppression caused by myeloid cells in the Tumor Microenvironment (TME)



OR2805-treated M2c macrophages promote T-cell activation, proliferation, recruitment and anti-tumor activity

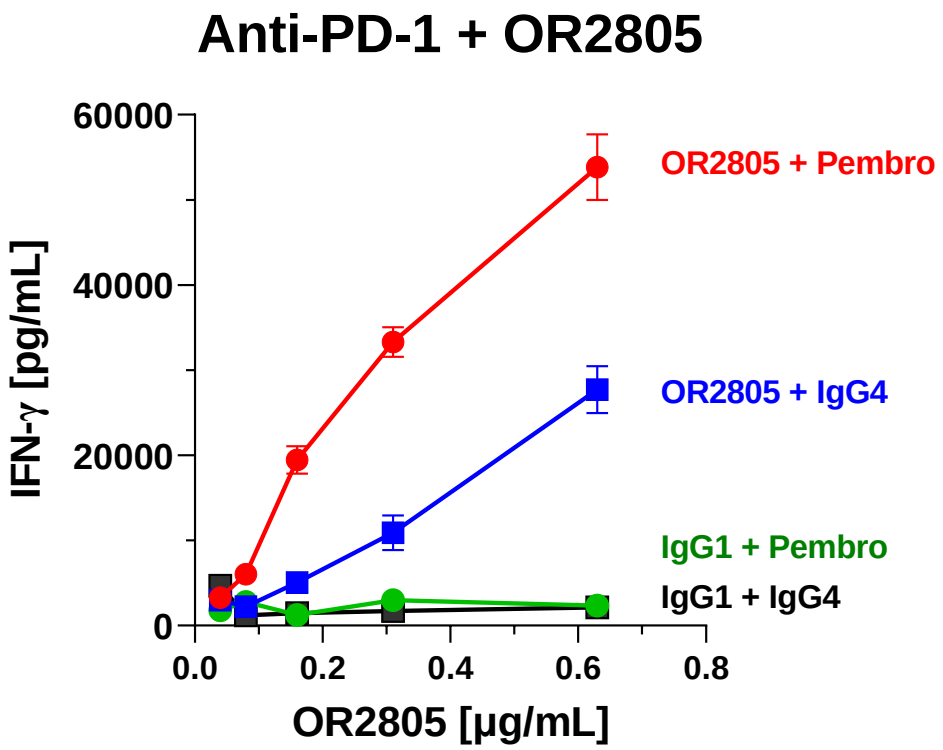


OR2805-treatment reduces the ability of M2c to suppress T-cell activation leading to greater T-cell stimulation (IL-2, IL-1β, IFNγ, TNFα, CCL4 & perforin production), and both $CD4^+$ and $CD8^+$ T-cell proliferation (2.5 to 5-fold increase)



OR2805-treated macrophages promote T-cell activation and recruitment and skewing to anti-tumor Th-1 phenotype

OR2805 restores anti-PD-1 activity of exhausted T cells

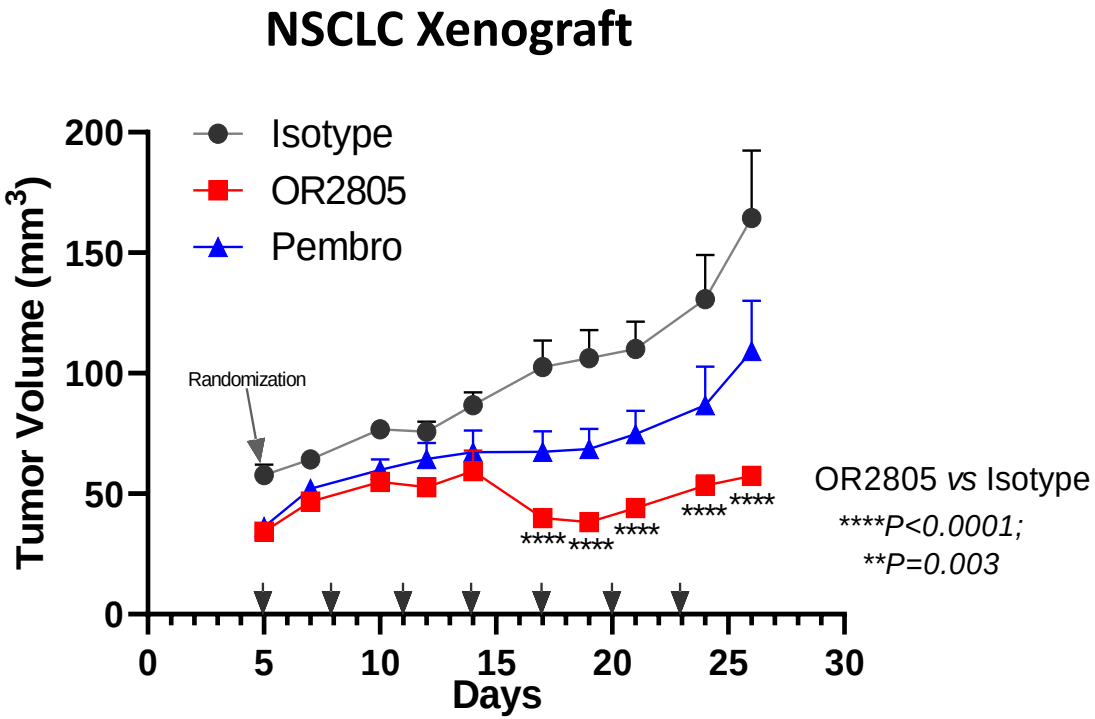


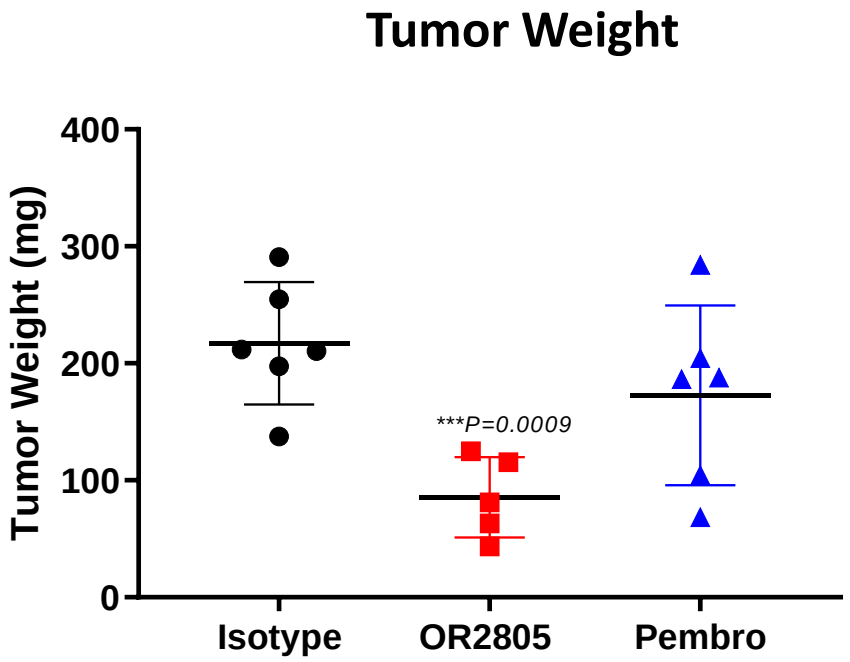
Vast Partnering Potential

Merck	*Keytruda (*pembrolizumab)
BMS	*Opdivo (*nivolumab)
Regeneron*	*Libtayo (*cemiplimab)
Roche	*Tecentriq (*atezolizumab)
AZ	*Imfinzi (*durvalumab)
Pfizer/M-S	*Bavencio (*avelumab)
GSK	*Jemperli (*dostarlimab)
Junshi	*Tuoyi* (toripalimab)
Beigene	BGB-A317 Tisle (tislelizumab)
Hengrui	*AiRuiKa* (camrelizumab)

*anti-PD-1 Supply Agreement executed July 2022

OR2805 anti-tumor activity is superior to anti-PD-1





OR2805-101 Phase 1/2 study

Part A: Dose-Escalation Solid tumors, no available therapies (N=54)

Cohort A1: OR2805 monotherapy
- Escalating IV doses of 150, 300, 600, 1200 mg every 3 weeks (complete)
- Escalating IV doses of 450 and 900 mg weekly

Cohort A2
OR2805
+ cemiplimab

Cohort A3
OR2805
+ docetaxel

Part B: Dose-Expansion NSCLC or melanoma (N=100)

Cohort B1
- NSCLC, progressed on immediately prior PD-1/PD-L1
- Randomized 1:1 to OR2805 or OR2805+cemiplimab (n=20 each)

Cohort B2
- NSCLC, at least 1 prior line of therapy and eligible for docetaxel
- All subjects receive OR2805+docetaxel (n=20)

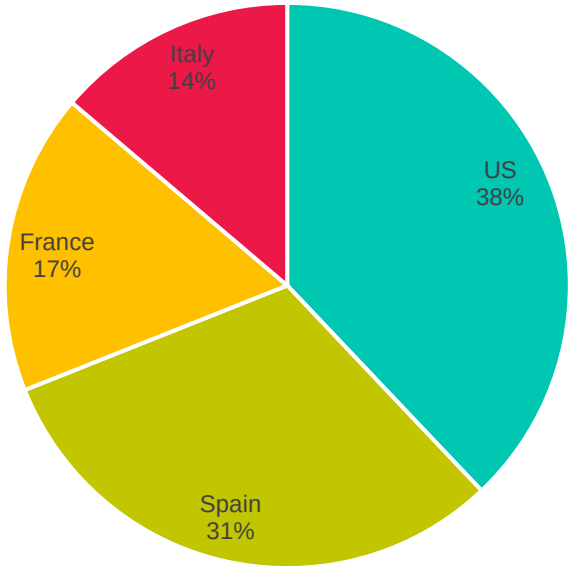
Cohort B3
- Melanoma, progressed on immediately prior PD-1
- Randomized 1:1 to OR2805 or OR2805+cemiplimab (n=20 each)

Part C: Biology Cohort (N=40)

Cohort C1
- Four separate tumor-specific subject populations
  - Liposarcoma
  - Leiomyosarcoma
  - SCCHN
  - Other tumor types
- OR2805 monotherapy at RP2D
- Pre- and on-treatment biopsies required
- 10 subjects in each disease indication

OR2805-101
Phase 2 Start Up Activities

- Phase 2 Start Up
  - 29 sites identified for participation
  - Global site distribution
    - 11 US
    - 9 France
    - 5 Spain
    - 4 Italy
  - 1st US site Activation Dec 2022
  - ROW Activations begin Feb/Mar



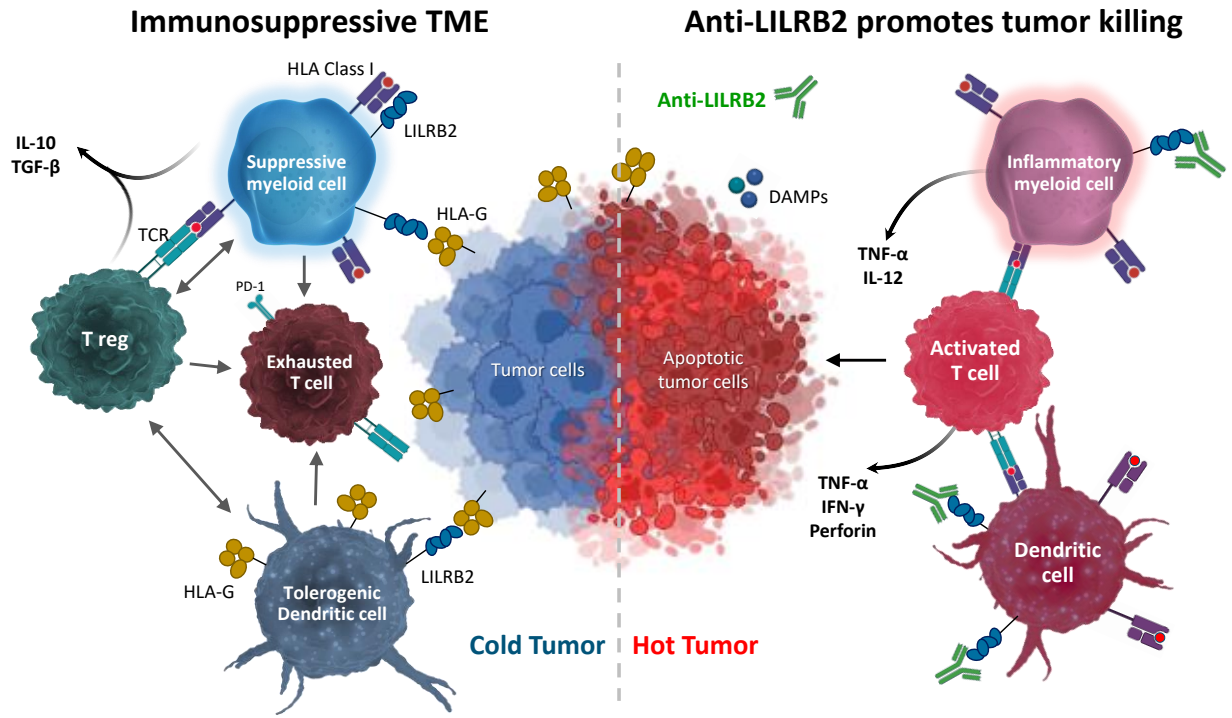
OncoResponse

Leukocyte Immunoglobulin Like Receptor B2 (LILRB2)

Targeting LILRB2–HLA-G binding to reverse immunosuppression in cancer

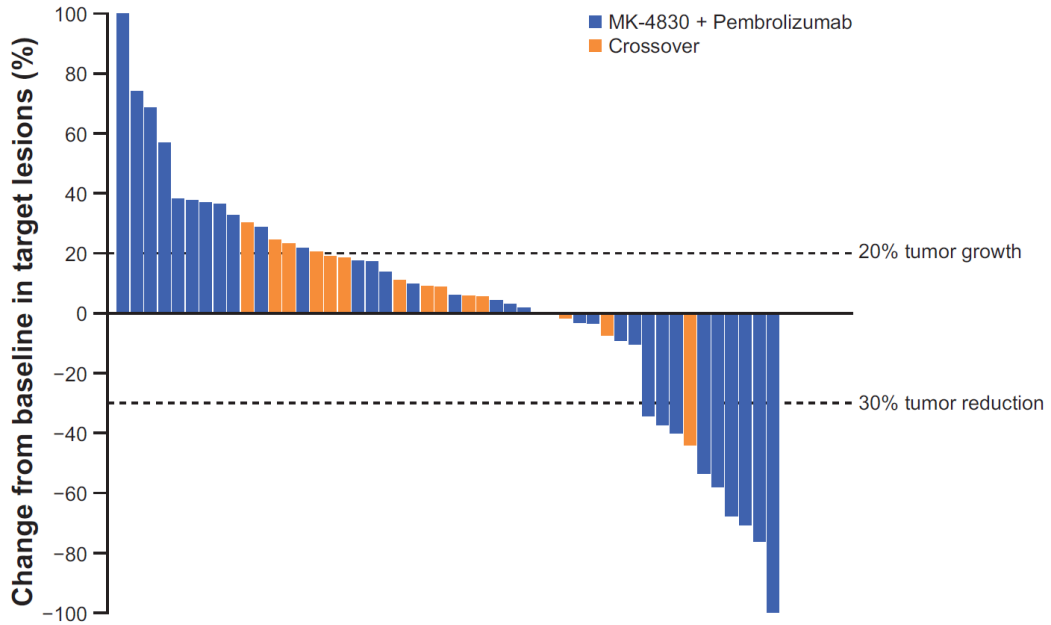
IND filing planned for Q2 2023

LILRB2 promotes immunosuppression and blockade drives clinical anti-tumor activity



- Inhibitory receptor on myeloid cells that contributes to CPI resistance
- Blockade reverses anti-PD-(L)1 resistance
- Expression correlates with poor survival in multiple cancers
- LILRB2 has multiple immune inhibitory activities

MK-4830 overall response in Phase 1



- MK-4830 is a clinically validated anti-LILRB2 antibody
- Monotherapy demonstrated one PR in ovarian cancer
- Combination with pembrolizumab demonstrated a 24% ORR
- 5 of 11 subjects with prior anti-PD-1 treatment responded to the combination

J Clin Invest. 2018;128:5647. Biochim Biophys Acta. 2018;1869:278. Clin. Cancer Res. 2021;28:57-70. J Immunol. 1998;160:3096-3100. Eur. J. Immunol. 1998;28:3423-34. Nat Immunol., 2002;3:237-43. PNAS 2003;100:8856-61.

OncoResponse OR502: Superior characteristics versus MK-4830

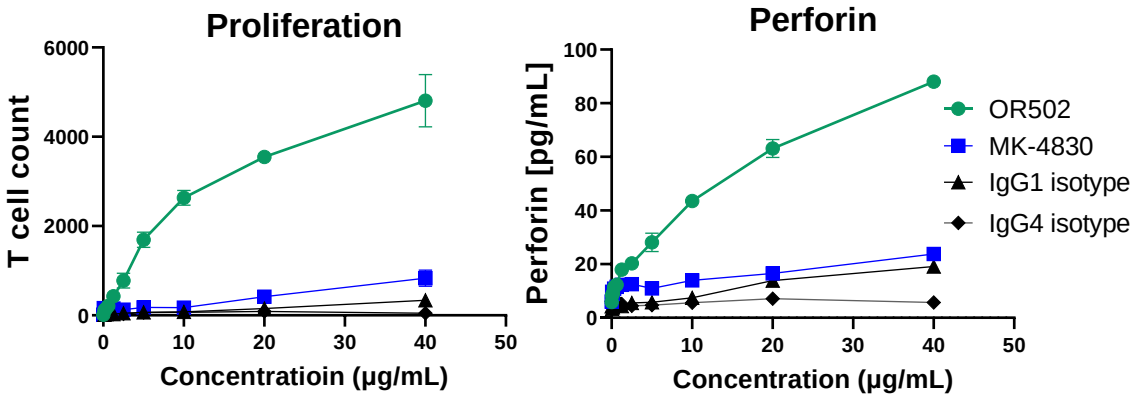
Criteria	OR502	MK-4830
Binding K_D to LILRB2	1.2 nM	3.5 nM
Blocks LILRB2 binding to HLA-G	Yes	Yes
Blocks LILRB2 binding to angiopoietin-like protein ligands 2 & 5	Yes	Yes
LILRB2 binding epitope	Distinct from other Abs	
Blocks LILRB2 binding to HLA Class I	**Yes**	No
Co-engagement of FcR	**Yes**	No
CD40L-mediated TNFα secretion by Macrophages	Yes	Yes
LPS-induced IFNγ secretion by human PBMC	**Strong**	Modest
T cell activation and proliferation (M2/T cell coculture)	**Yes**	No
IFNγ production (M2/Exhausted T cell coculture)	**Yes**	No
SK-MEL-5 xenograft in humanized NSG-SGM3 mice	**79% TGI** **33% Regression**	26% TGI 11% Regression

OR502 is safe and restores anti-cancer T cell responses better than MK-4830

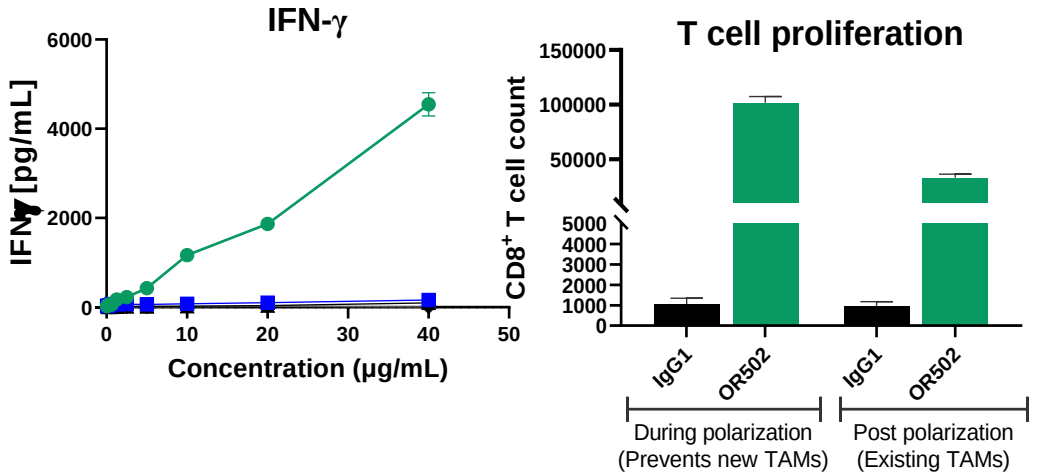
Amplifies anti-PD-1 activity in M2/T cell coculture assays

M2c/T cell coculture

(Rescues T cell proliferation and activation)

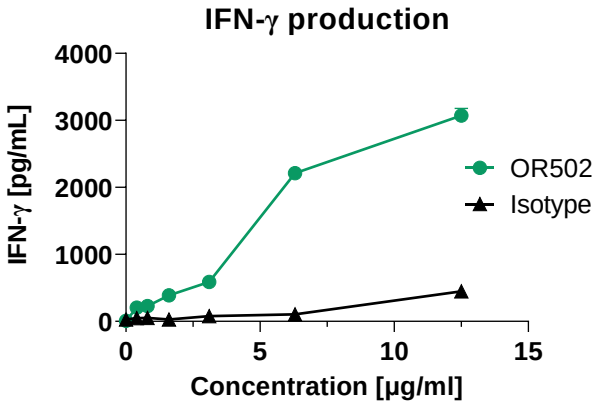


(Reduces and prevents immunosuppressive phenotype of existing and new TAMs)

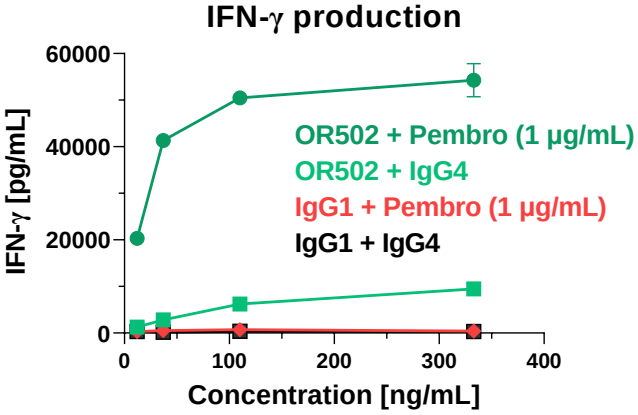


M2c/Exhausted T cell coculture

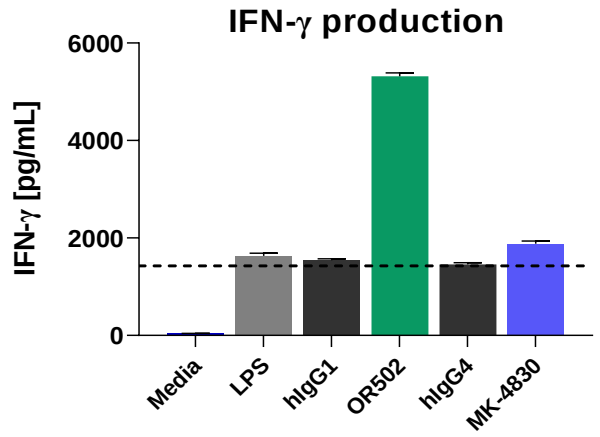
(Rescues IFN-γ production)



(Amplifies anti-PD-1 activity)

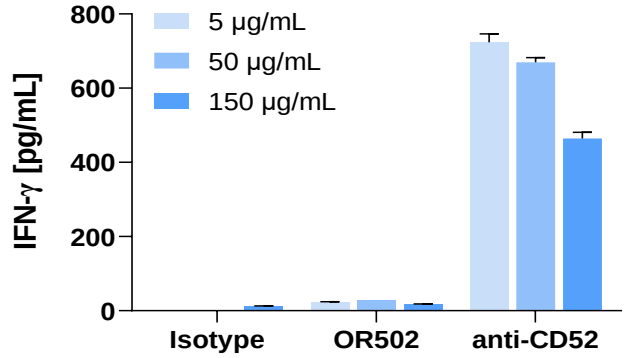


Boosts LPS-induced IFN-γ secretion



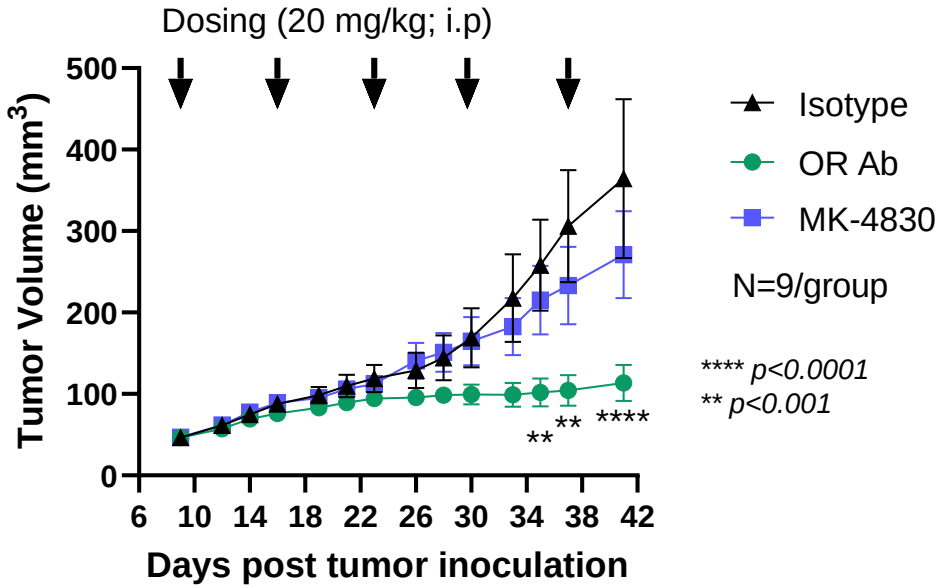
Whole blood cytokine release

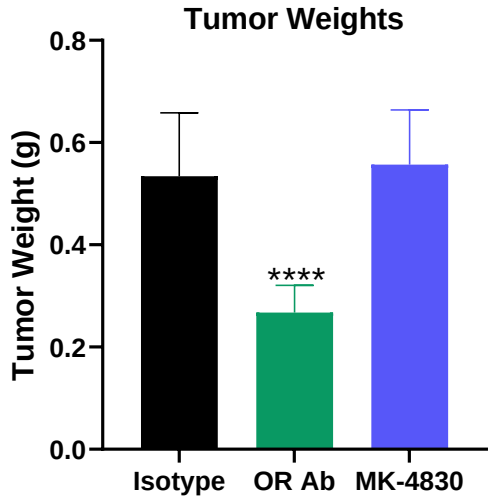
(Minimal or no risk of cytokine release syndrome)



OR502 parent antibody demonstrates significant anti-tumor activity

OncoResponse anti-LILRB2 antibody significantly inhibits growth of SK-MEL-5 melanoma in NSG-SGM3 mice





	Tumor Growth Inhibition (%)						Regression (%)
Group	***d28***	***d30***	***d33***	***d35***	***d37***	***d41***	***d41***
Anti-LILRB2 (OncoResponse)	47	57	69	74	78	79	33
MK-4830 (Merck)	-5	3	16	17	24	26	11

OncoResponse pipeline summary

ANTIBODY	Mechanism	Discovery	IND-Enabling	Phase 1	Phase 2
OR2805	Reprograms TAMs/MDSCs				
Anti-LILRB2/ILT4	Reverses immunosuppression & reprograms TAMs				
TME 2.0	Interrogate B-cell repertoire for mAb candidates				

- Lead drug OR2805 advancing through clinical studies across multiple tumor types
- Several antibodies in development that modulate immune cell activity
- Platform for ongoing discovery of rare human antibodies from Elite Responders

Abbreviations: TAM, tumor-associated macrophage; MDSC, myeloid-derived suppressor cell; mAb, monoclonal antibody

OncoResponse

Interrogating for **Cures**™

ThankYou.

For more information, please visit
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cstocks@oncoresponse.com