GNUBIOTICS SCIENCES

DECIPHERING THE TUMOR GLYCOCODE

Swiss Biotech Day 2024

22nd – 23rd April

CONFIDENTIAL

www.gnubiotics.com

Gnubiotics Introduction

COMPANY OVERVIEW

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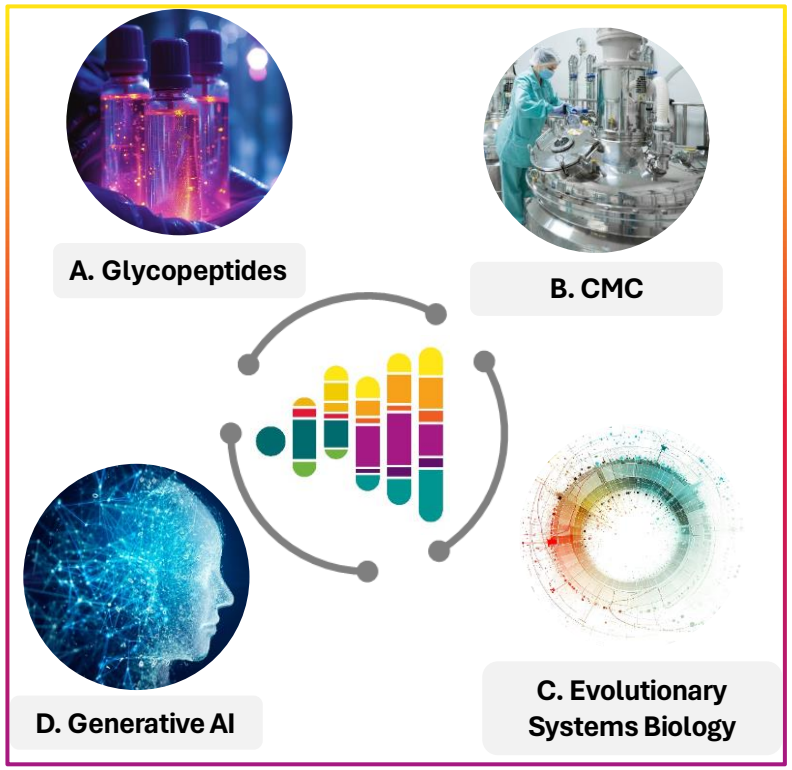
Gnubiotics is a Swiss biotech developing its platform GENESIS™ developed a novel platform of O-linked glycopeptide innovation opening a new universe of glycan-based therapies with far reaching applications in many biological systems. These glycopeptides have already demonstrated biological proof of principle in activating 3 major biological systems: the adaptive immune system, regulating chronic inflammation, and preserving and restoring the microbiome to a healthy state.

- **Established**: 2016
- **Headquarters**: Lausanne, Switzerland
- **Current Team**: 15
- **Lab space & lab capabilities**: Superlab Suisse (Biopôle)
  - Analytical Chemistry | Microbiology | Genetic Sequencing | Molecular biology / PCR | Mass Spectrometry

Gnubiotics has mastered the intelligent (rational) design and manufacturing of precise complex glycopeptide biologics that target and affect the aforementioned biological systems. This has resulted a robust pipeline of first-in-class (novel therapeutics) that are able to activate the adaptive immune system in a range of cancers with an unprecedented safety profile.

Gnubiotics GENESIS Platform

GENESIS is a revolutionary platform at the intersection of four cutting-edge technologies developed at Gnubiotics. With its multidimensional approach, GENESIS holds the promise to reshape the landscape of medical research, offering hope and tangible advancements in the fight against complex diseases, ushering in a new era of tailored treatment strategies.



GENESIS' 4 cutting edge technologies:

A. **Glycopeptides:** mastered the rational design and development of a series of important biologic therapeutics.

B. **CMC:** mastered a unique and proprietary method to produce at ton scale and to further manufacture all its biologics therapeutics.

C. **High-Resolution Sequencing:** developed important technologies from its high-res sequencing capabilities to ID key predictive biomarkers.

D. **Generative AI:** Biomarker activity is leading to a material database where generative AI is being applied to further predict, discover, and develop new therapeutic opportunities.

Key Investment Highlights

INTRODUCTION

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A new class of glycopeptide biological therapeutic

-Activates the body's adaptive immune system

-Orally available and stable through the GI tract into the large bowel.

-Very favorable safety profile emerging

-Ton-scaled production capability and capacity.

Differentiated and demonstrated Mechanism of Action (MoA)

-Activation of the adaptive immune system exposing cold tumors for T-cell eradication

-Demonstrated activation of dendritic cells

-Demonstrated tumor-specific priming of CD8 T-cells (IP filing in process)

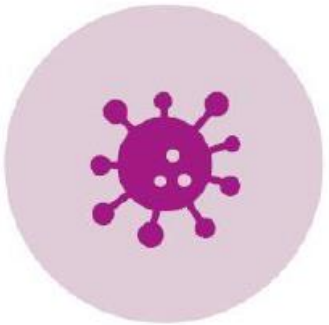
Efficacy in immunotherapy (I/O)-resistant tumors

-Extensive preclinical testing demonstrating strong Proof of Concept activity.

-Multiple epithelial tumors tested showing consistent efficacy in I/O-resistant tumors

-Synergistic results in combination with I/O therapy

-Lead Indication, Microsatellite Stable (MSS) CRC with critical unmet patient needs



Novel tumor differentiating biomarkers The Tumor Glycocode

-Deciphering tumor surface aberrant glycan profiles

-Distinguishing tumor cells from healthy cells

-Distinguishing tumor subtypes, i.e., MSS versus MSI (Microsatellite Instability) CRC

-Meaningful differential diagnosis for patient stratification and treatment

-Deployable to laboratories performing tumor biopsies

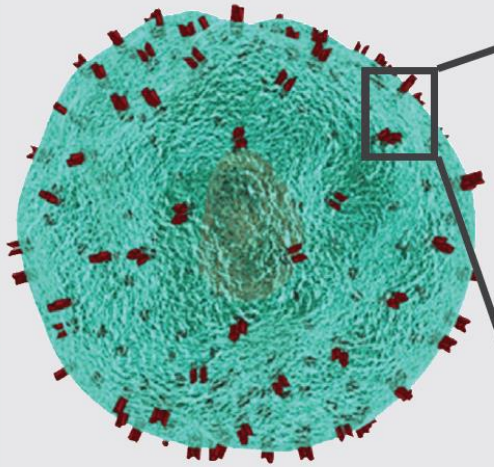
GNU101: Clinical Strategy targeting hard-to-treat patients

RATIONALE CRC

- When CRC has metastasized, the 5-year survival rate is <15% in the USA, thus more effective treatments are needed.
- Immune checkpoint inhibitors are only effective so far in the **minority of patients** with dMMR–MSI-H CRC tumors.
- **ICI response rate is low** (40%) in patients with dMMR–MSI-H CRC tumors and must be given intravenously, leading to frequent visits to hospitals.

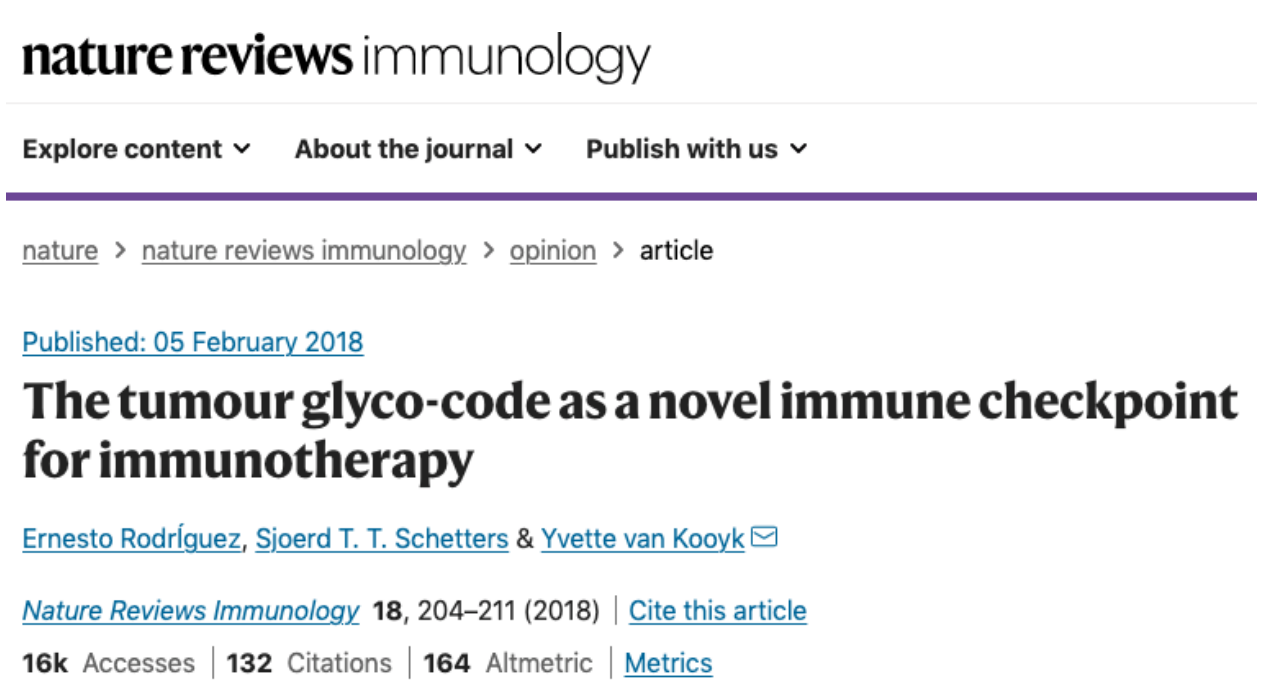
Traditional immunotherapy

dMMR–MSI-H 15% CRC cases	pMMR–MSI-L 85% CRC cases
Only 4% of metastatic CRC cases are MSI-H	*Vast majority of patients with metastatic CRC*
ICI Response Rate 40%	**ICI Response Rate** Largely unresponsive
Anti-PD1 approved as first-line treatment of advanced MSI-H/dMMR CRC	*Anti-PD1 not approved yet*



Abundant & aberrant glycan profile is a signature of cancer development.

Glycopeptides in Oncology: Multiple Immuno-Targets to be Exploited



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Published: 05 February 2018

The tumour glyco-code as a novel immune checkpoint for immunotherapy

Ernesto Rodríguez, Sjoerd T. T. Schetters & Yvette van Kooyk

Nature Reviews Immunology **18**, 204–211 (2018) | Cite this article

16k Accesses | **132** Citations | **164** Altmetric | Metrics

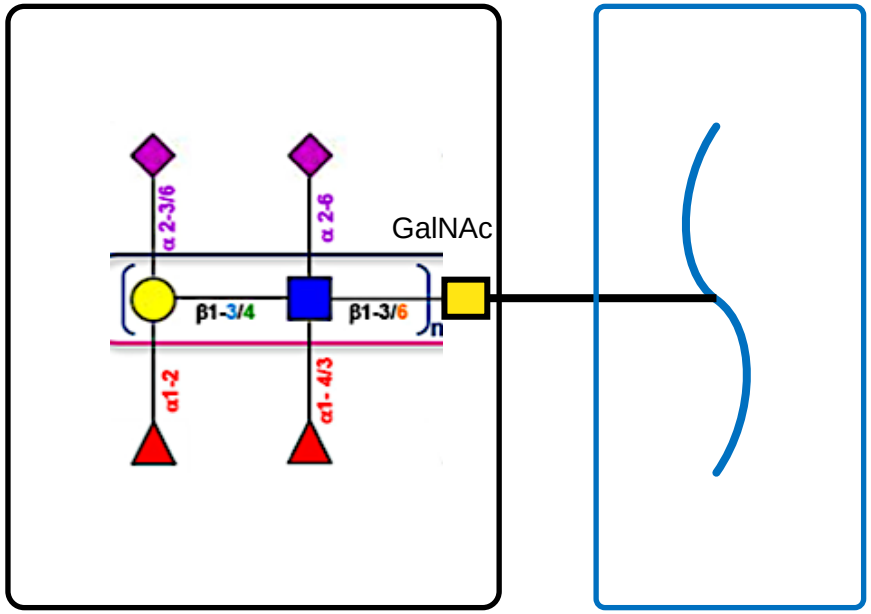
"The role of tumor glycosylation in immune evasion has mostly been overlooked"

- **IMMUNO-MODULATORS**: specific glycan signatures found on tumor cells can be considered as a novel type of immune checkpoint.
- **IMMUNO-TARGETS**: glycosylation of tumor proteins generates neo-antigens that can serve as targets for tumor-specific T cells.

Source: https://www.nature.com/articles/nri.2018.3

GNU101: Ensemble of O-glycan / Peptide Conjugates

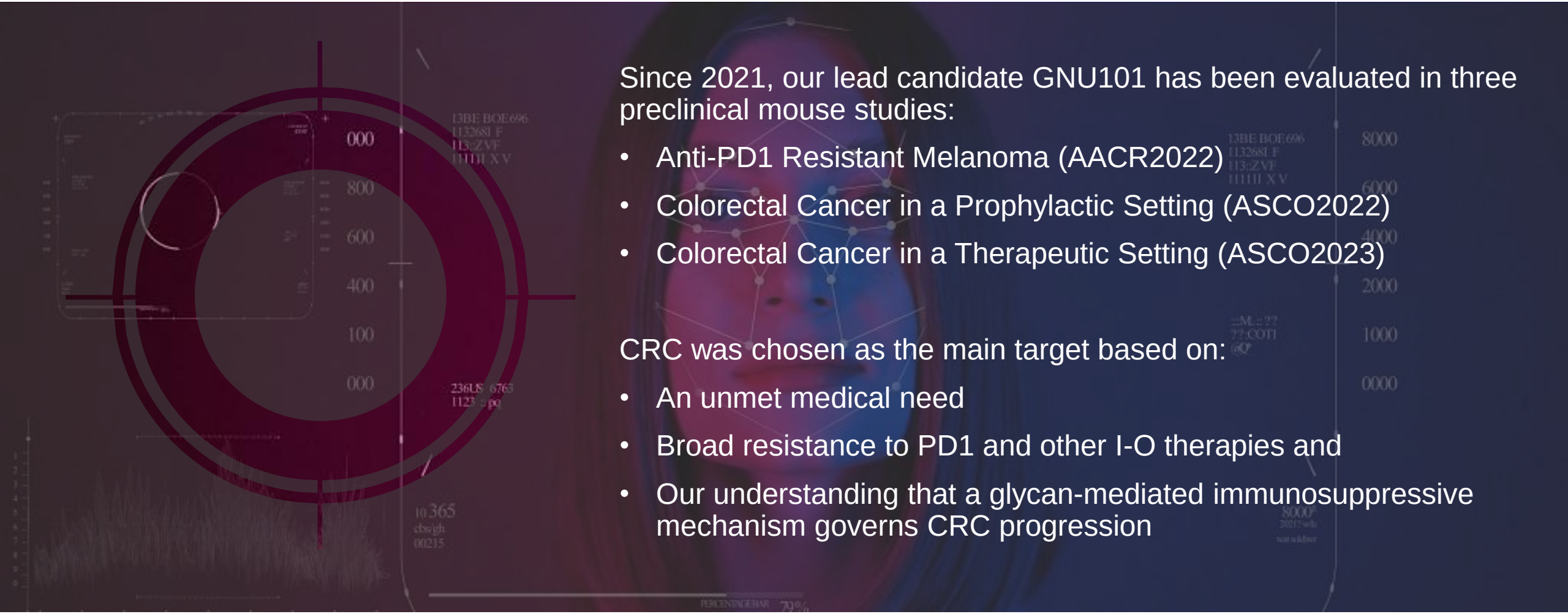
GNU101



O-Glycan ---- **Peptide**

Glycan structure	MSI-H	MSS	GNU101
core 1 O-glycans	↓	↑ (P=0.026)	+
terminal α2-3 sialylation of Gal	↓	↑ (P=0.0028)	+
sialyl-3-T	↓	↑ (P=0.059)	+
disialyl-T	↓	↑ (P=0.035)	+

Preclinical Studies and History



Since 2021, our lead candidate GNU101 has been evaluated in three preclinical mouse studies:

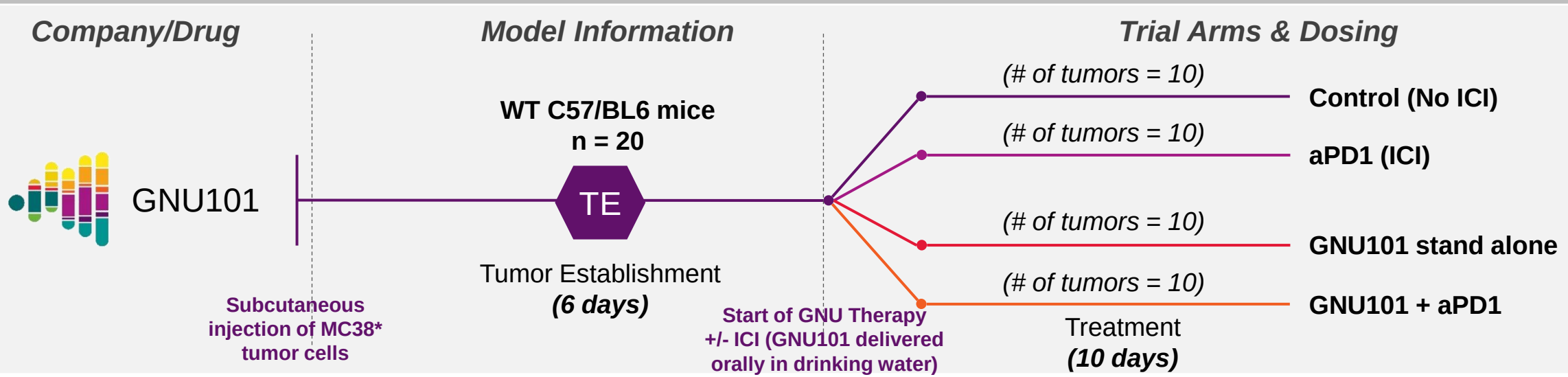
- Anti-PD1 Resistant Melanoma (AACR2022)
- Colorectal Cancer in a Prophylactic Setting (ASCO2022)
- Colorectal Cancer in a Therapeutic Setting (ASCO2023)

CRC was chosen as the main target based on:

- An unmet medical need
- Broad resistance to PD1 and other I-O therapies and
- Our understanding that a glycan-mediated immunosuppressive mechanism governs CRC progression

Efficacy of Target Specific Glycopeptides in a Therapeutic Model of CRC

PRECLINICAL THERAPEUTIC MODEL: CRC



Primary Endpoints:

- Tumor volume: to demonstrate tumor volume reduction (measured every 3 days).
- Tumor weight: to demonstrate tumor weight reduction (measured at day 16).

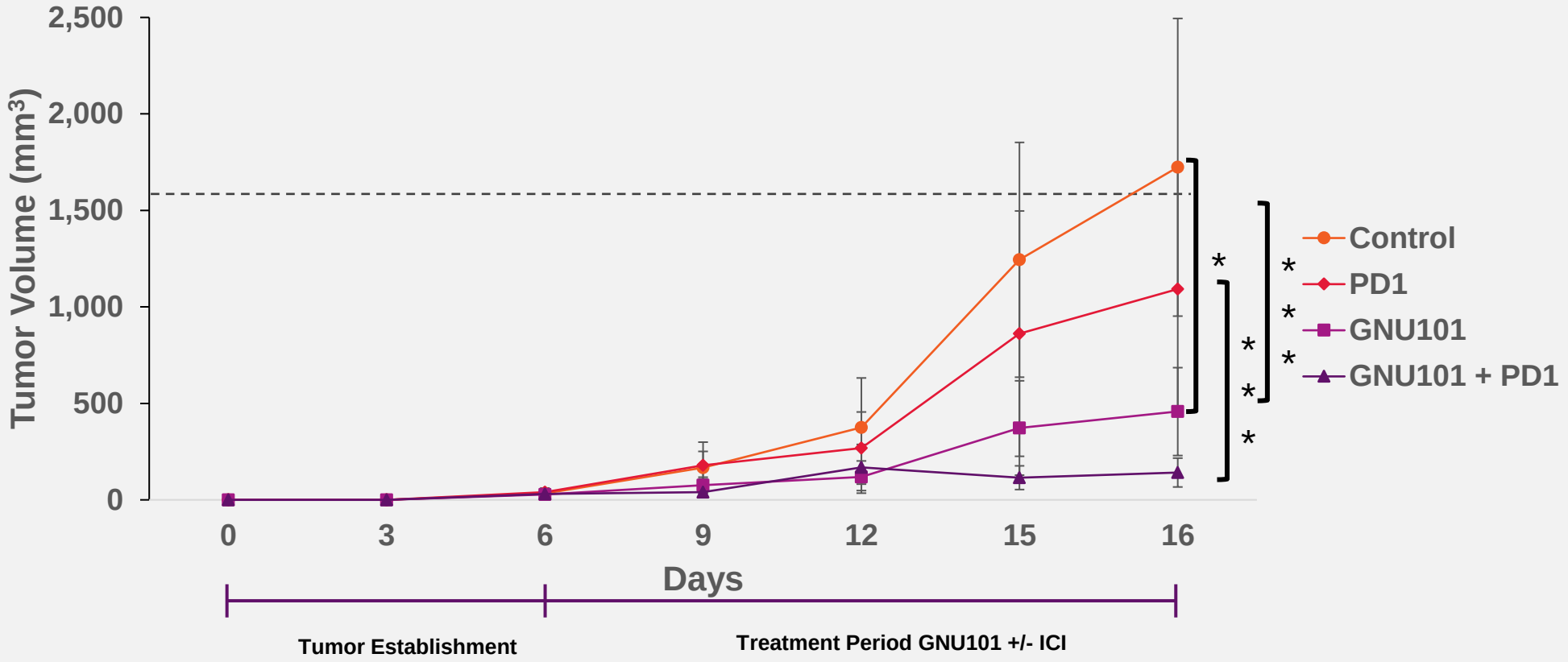
Secondary Endpoints:

- Tumor Infiltrating Lymphocytes (TILs) & subsets: (measured at day 16).

*** MC38 were shown to have intermediate Tn antigen levels**

GNU101 Shown to Reduce CRC Tumor Volume in a Therapeutic Model

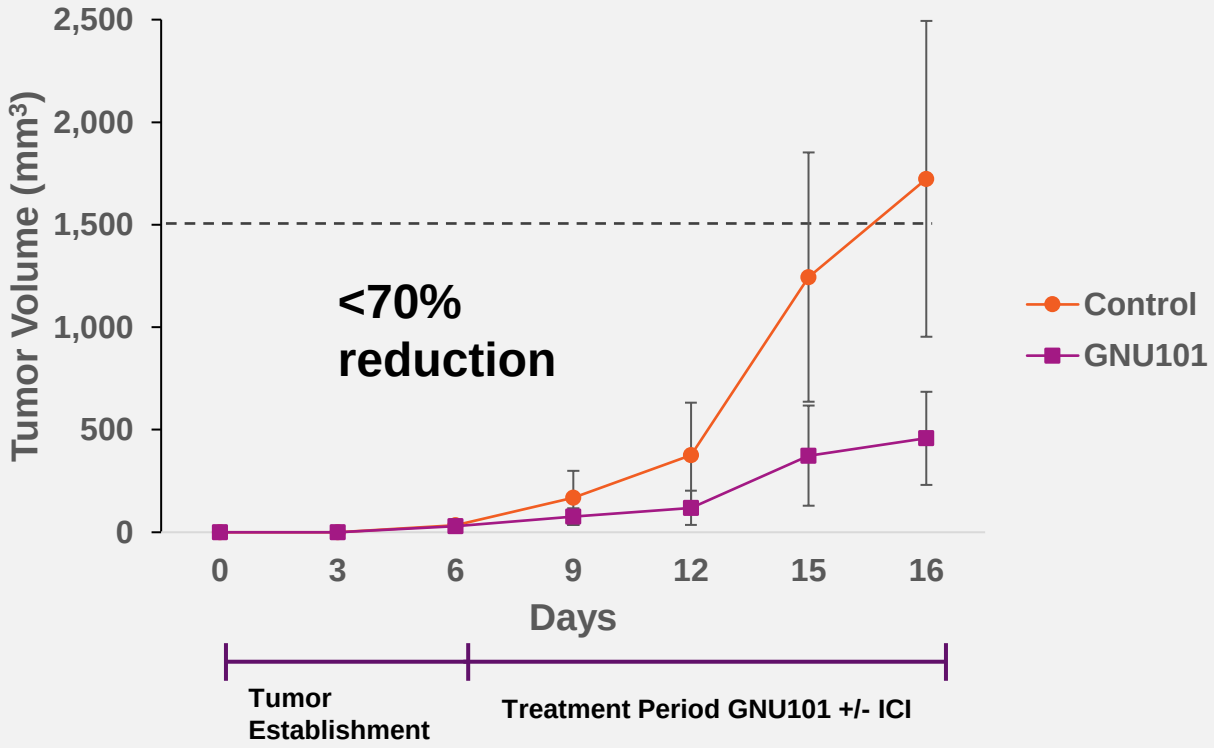
PRECLINICAL THERAPEUTIC MODEL: CRC

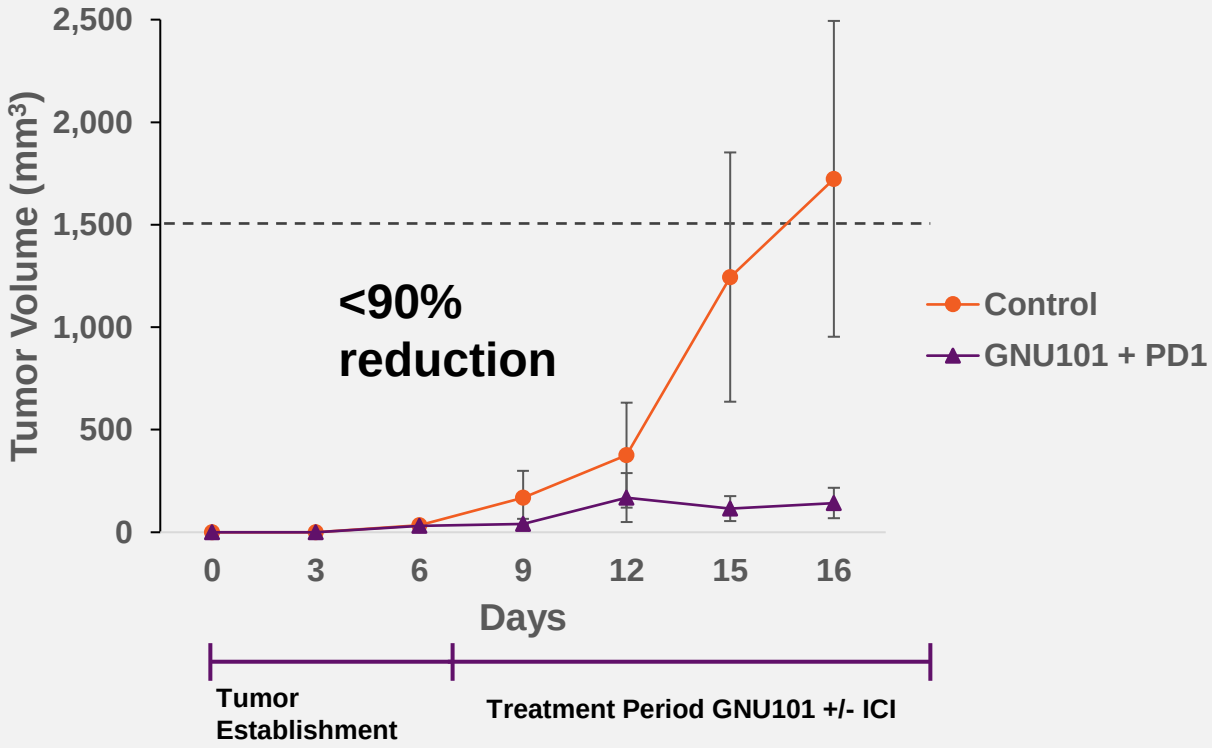


*Dashed line: termination criteria, *p<0.05, ***p<0.001*

GNU101 in Combination with aPD1 Shown to Additively Reduce CRC Tumor Volume

PRECLINICAL THERAPEUTIC MODEL: CRC

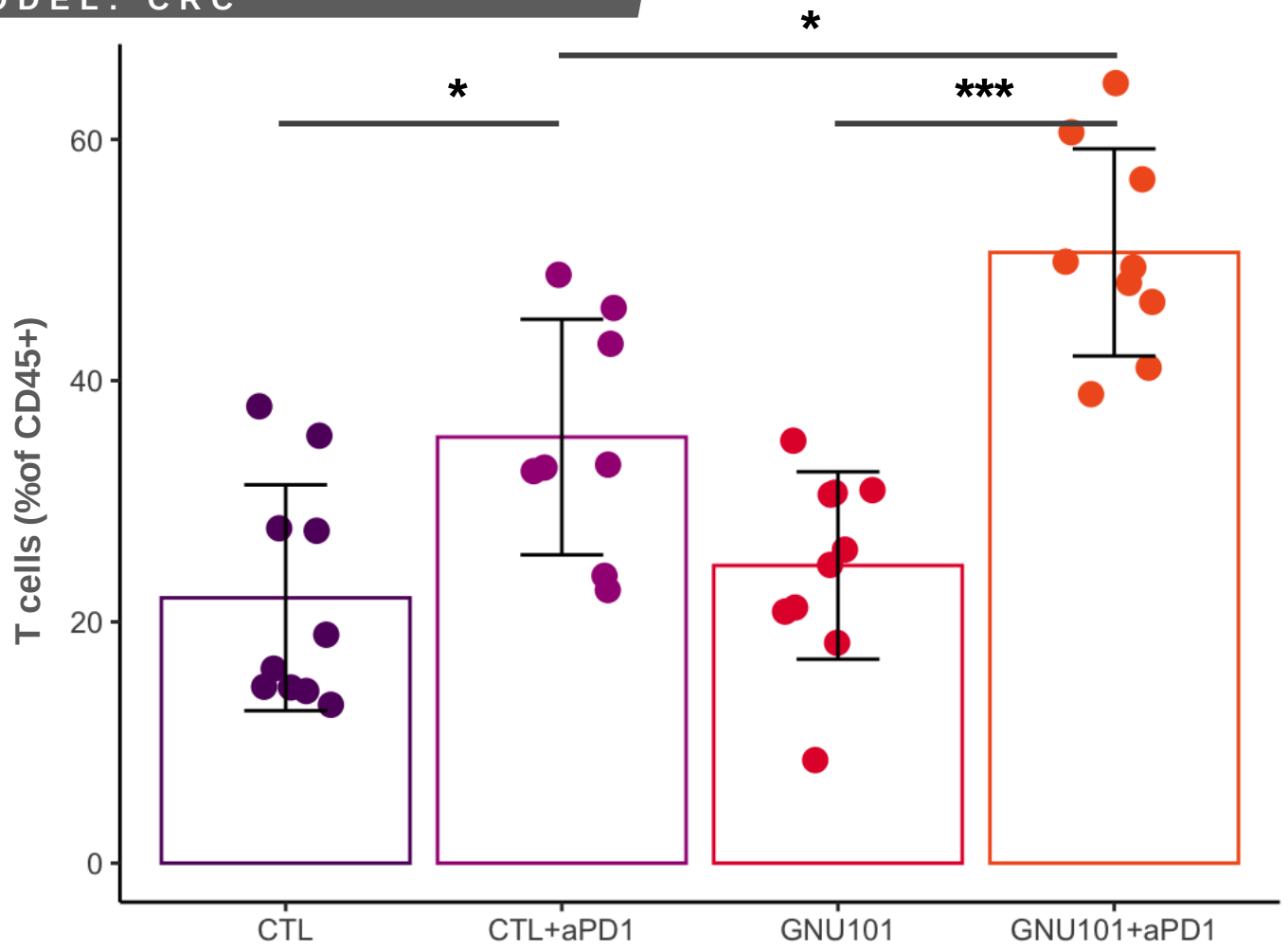




*Dashed line: termination criteria, *p<0.05, ***p<0.001*

GNU101 Turns a Cold Tumor Environment into a Hot Tumor Environment

PRECLINICAL THERAPEUTIC MODEL: CRC

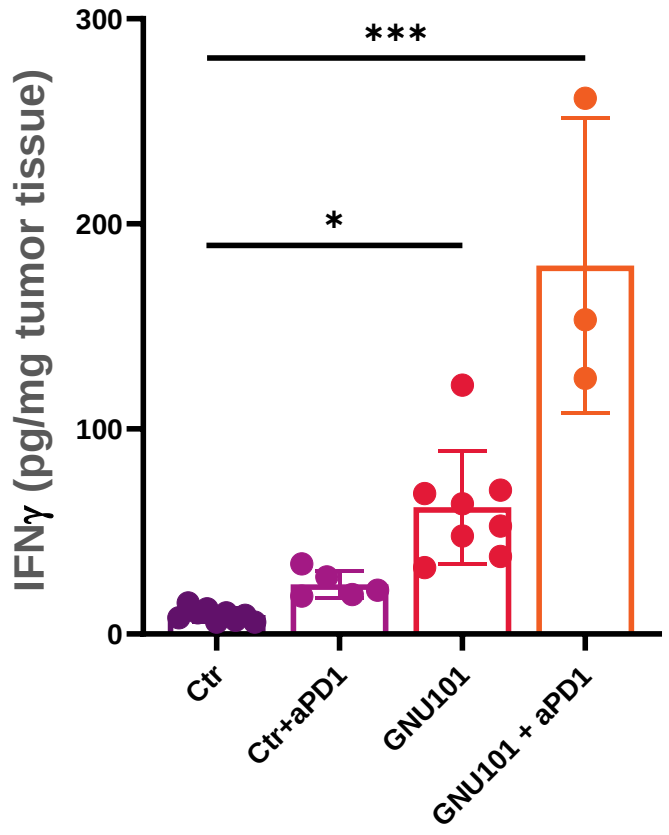


- **Helps Increase Expansion & Infiltration of T cells in the Tumor**
- Increase in infiltrating T cells & cytotoxic T cells

p<0.05, ***p<0.001

GNU101 Modulates CD8 Tc Pro-inflammatory Cytokines IFNγ within the TME

PRECLINICAL THERAPEUTIC MODEL: CRC



- IFN-γ is a potent proinflammatory cytokine and effector molecules of anti-tumor immunity.
- Higher levels of IFN-γ are consistent with elevated activation of CD8 T cells by GNU101.

p<0.05, ***p<0.001

GNU101 Decreases IL-10 within the TME

PRECLINICAL THERAPEUTIC MODEL: CRC

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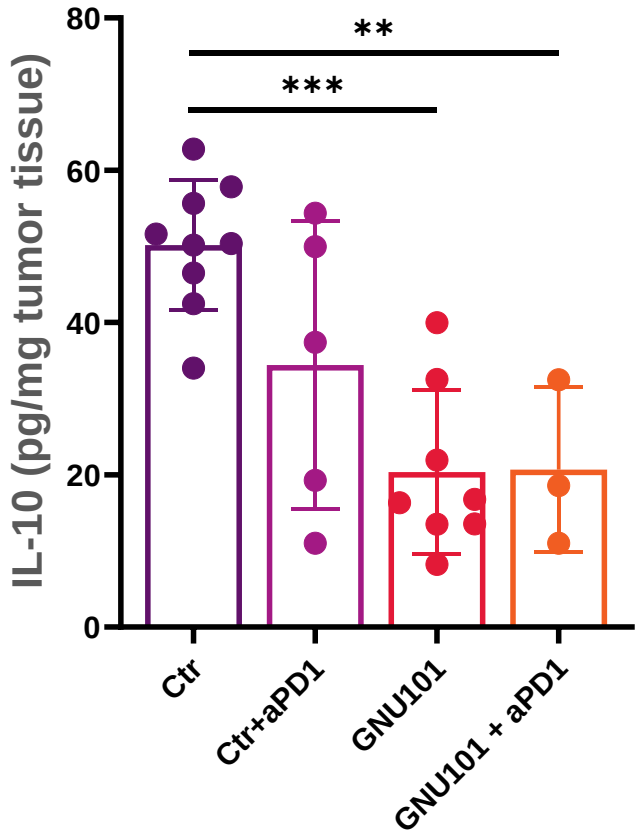

- decreased IL-10 levels indicate a generally more inflammatory but also more potent anti-tumor environment.
- IL-10 was found in mice treated with GNU101 signifying alleviation of immunosuppression.

p<0.01, ***p<0.001

GNU101 Enables a Statistically Significant Reduction of Tim3+ CD8 in Both Monotherapy and in Combination with aPD1

PRECLINICAL THERAPEUTIC MODEL: CRC

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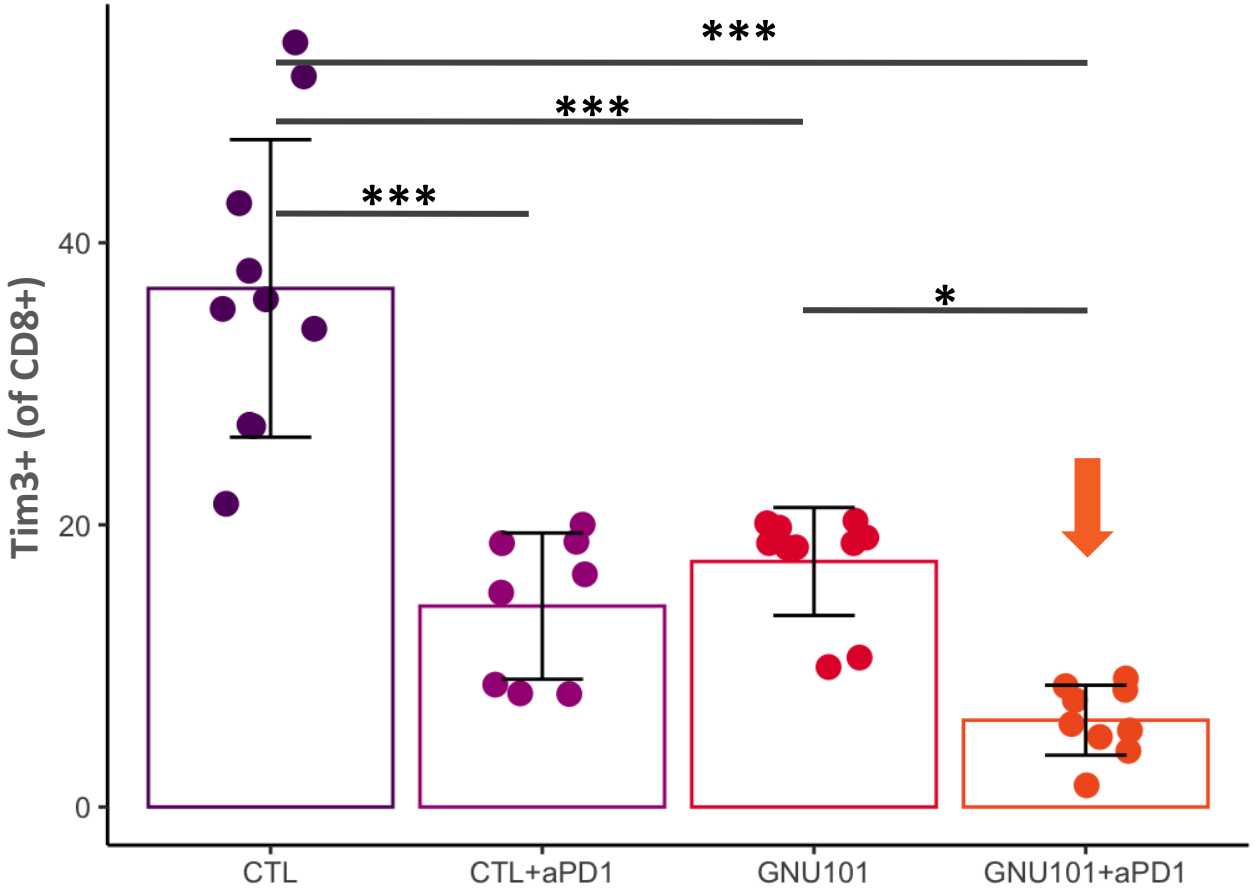

- Tim3+ is a potent suppressor of immune response.
- Tim3+ is a checkpoint inhibitor and a marker of exhausted T cells (loss of ability to kill).

p<0.05, ***p<0.001

Efficacy of Target Specific Glycopeptides in a CRC Eradication Study

LONG DURATION MODEL CRC

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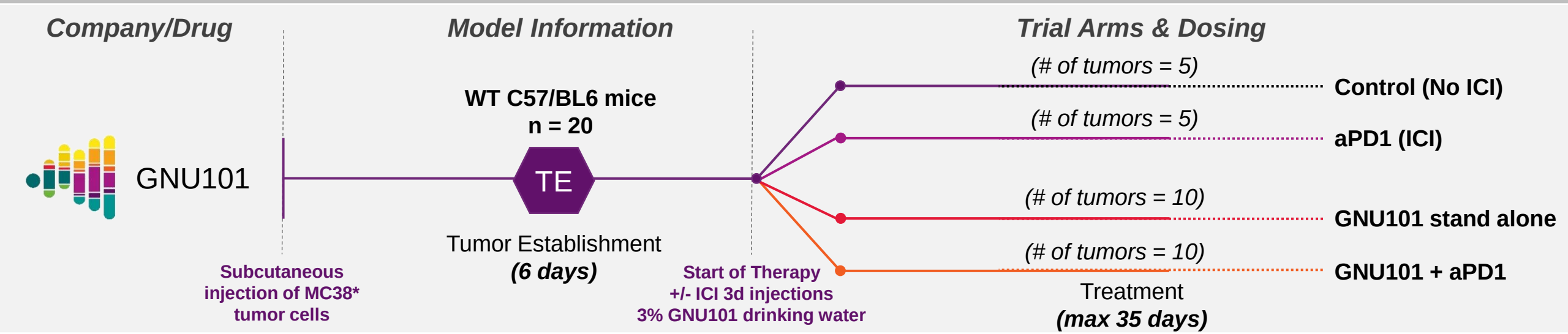


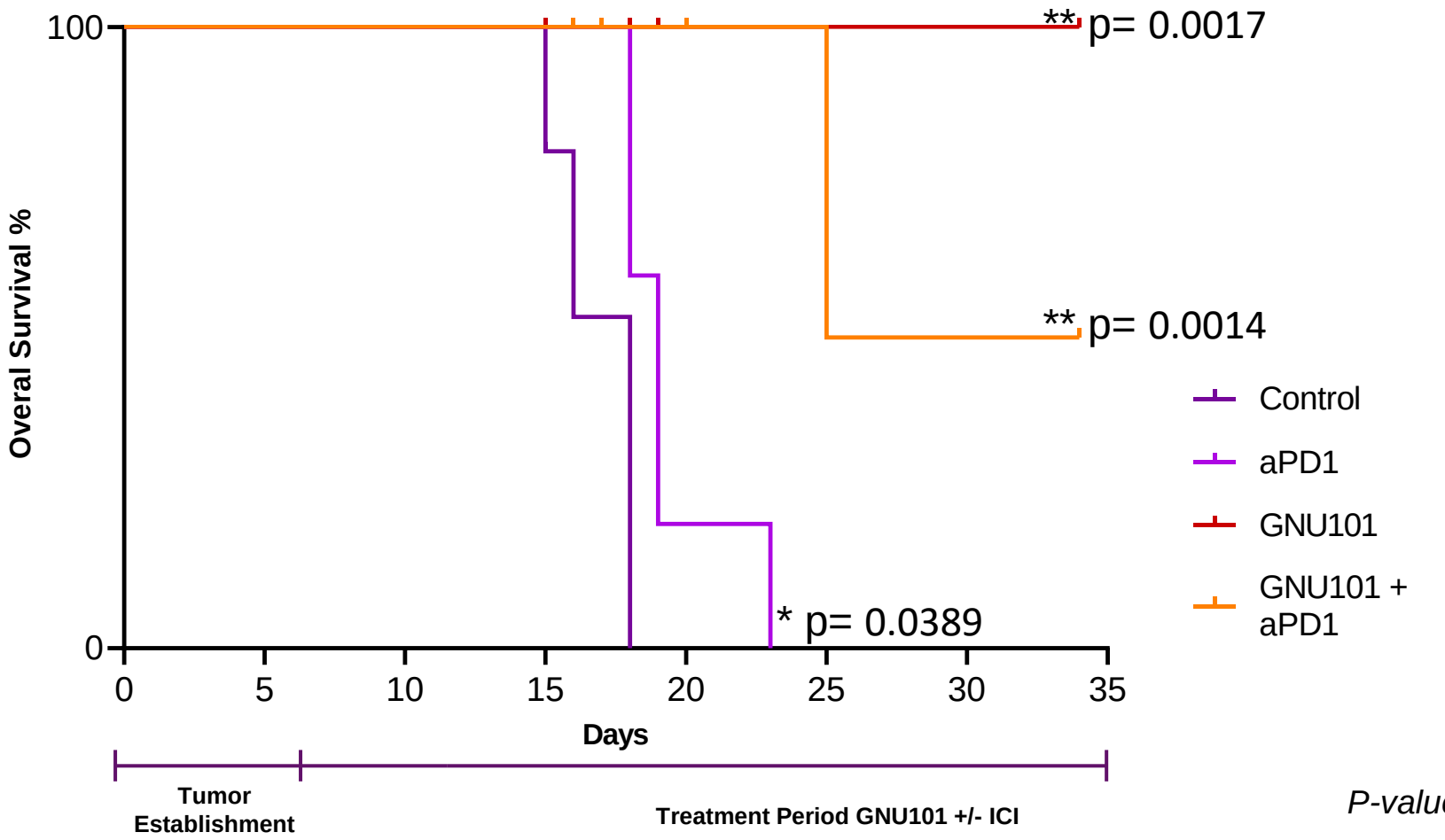
Primary Endpoints:

- Tumor volume: to demonstrate tumor volume changes (measured every 3 days).
- Overall Survival

*** MC38 were shown to have intermediate Tn antigen levels**

GNU101 glycopeptides delay both the onset and limit tumor growth

LONG DURATION CRC



- GNU only, aPD1 only, or GNU+aPD1 leads to enhanced survival/reduced risk to die from tumor burden.
- p=0.0088 (aPD1 vs GNU+aPD1) concludes that the anti-tumor effect of GNU101 is bigger than the effect of ICI

*P-values compared to control, *p<0.05, **p<0.01*

Team

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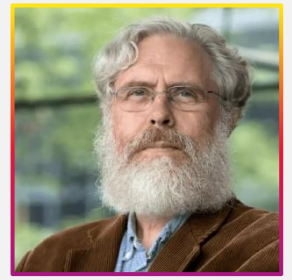

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