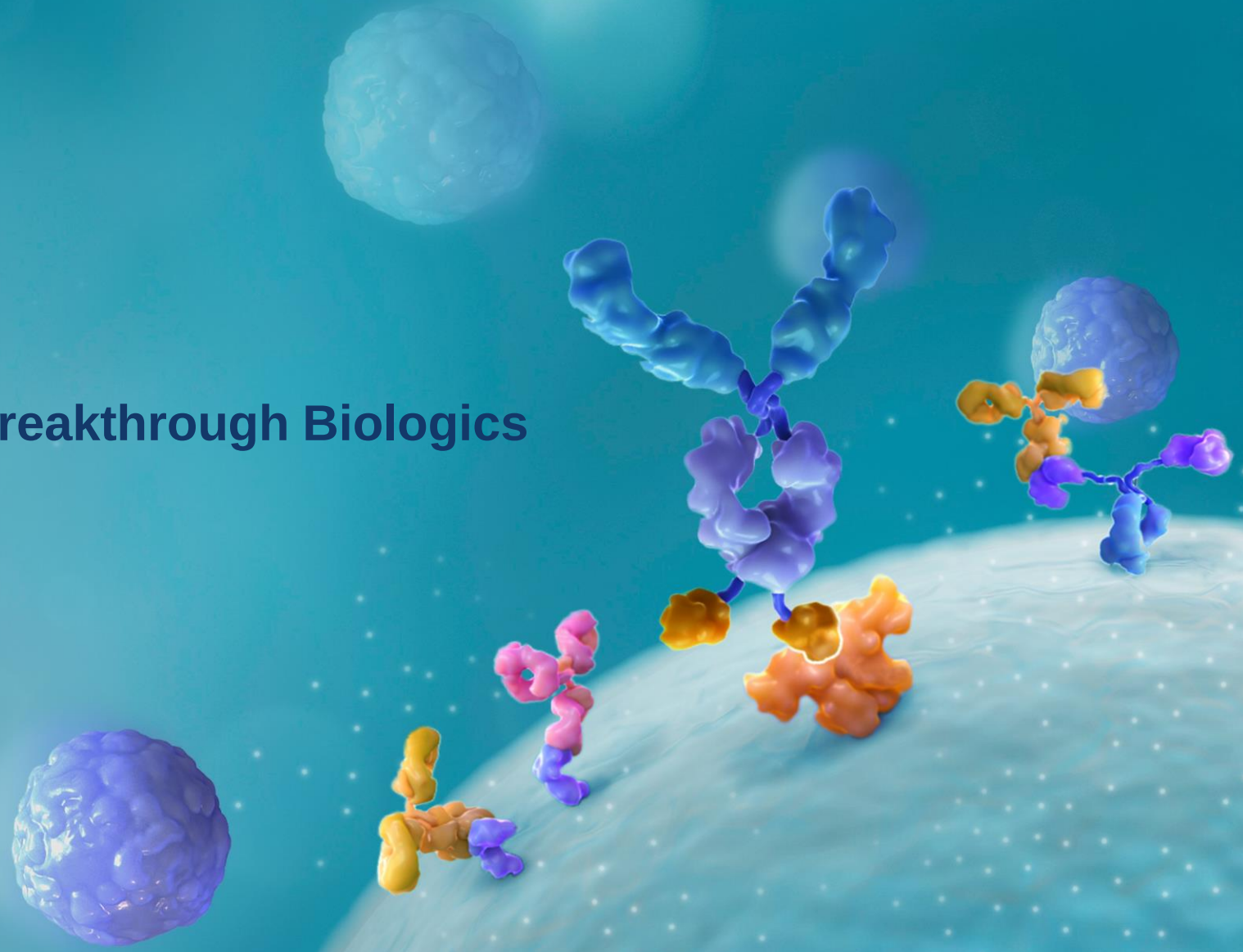
GI Innovation

Innovative Healthcare with Breakthrough Biologics



2017~2018

Jul 2017	Founded
May 2018	Strategic Partnership with Samsung Biologics

2018~2021

Nov 2019	Out-licensing of GI-101 to Simcere, China For $ 790M in the Greater China Region
Jul 2020	Out-licensing of GI-301 to Yuhan, Korea For $ 1.2B Excluding Japan (Sublicensing, 50/50 Profit Sharing)
Jul 2020	Collaboration with MSD for GI101·Keytruda®
Jun 2021	GI-101 Ph I/II IND (US, KR)
Jul 2021	GI-301 Ph I IND (KR)
Nov 2021	Collaboration with AstraZeneca GI-101·Imfinzi®

2022~

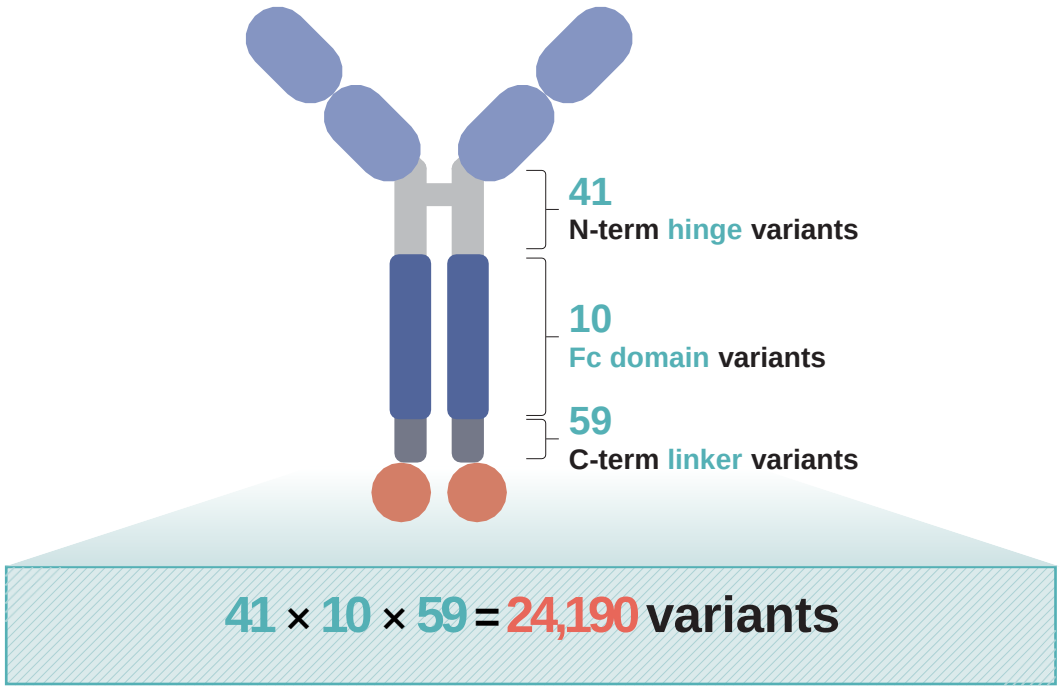
May 2022	GI-101 Ph I/II Granted $ 5.8M from Korea Drug Development Fund (KDDF)
Sep 2022	GI-108 Granted $ 1.7M from KDDF
Oct 2022	GI-101 Orphan Drug Designation (US FDA)
Feb 2023	GI-102 Ph I/IIa IND (US/KR)
Mar 2023	Listed in KOSDAQ

Applied USD/KRW: 1,200

GI-SMART™ Platform Technology for Accelerated Development of Bispecific Proteins

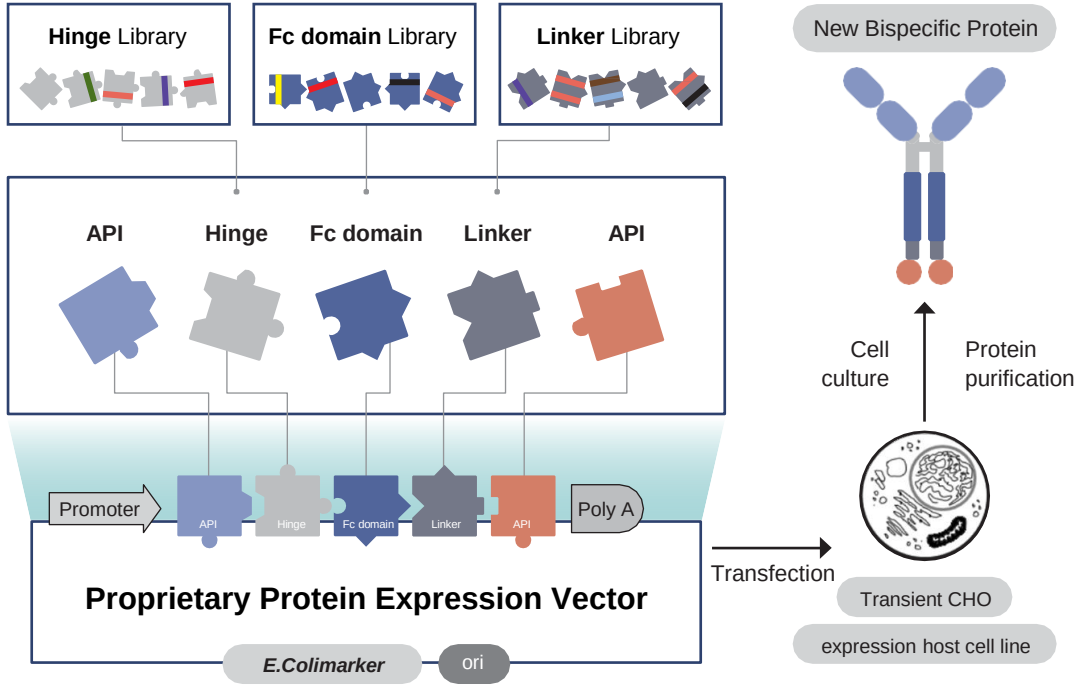
SMART-Selex™

Libraries for specific of bispecific proteins
Enable quick assembly of stable and functional proteins

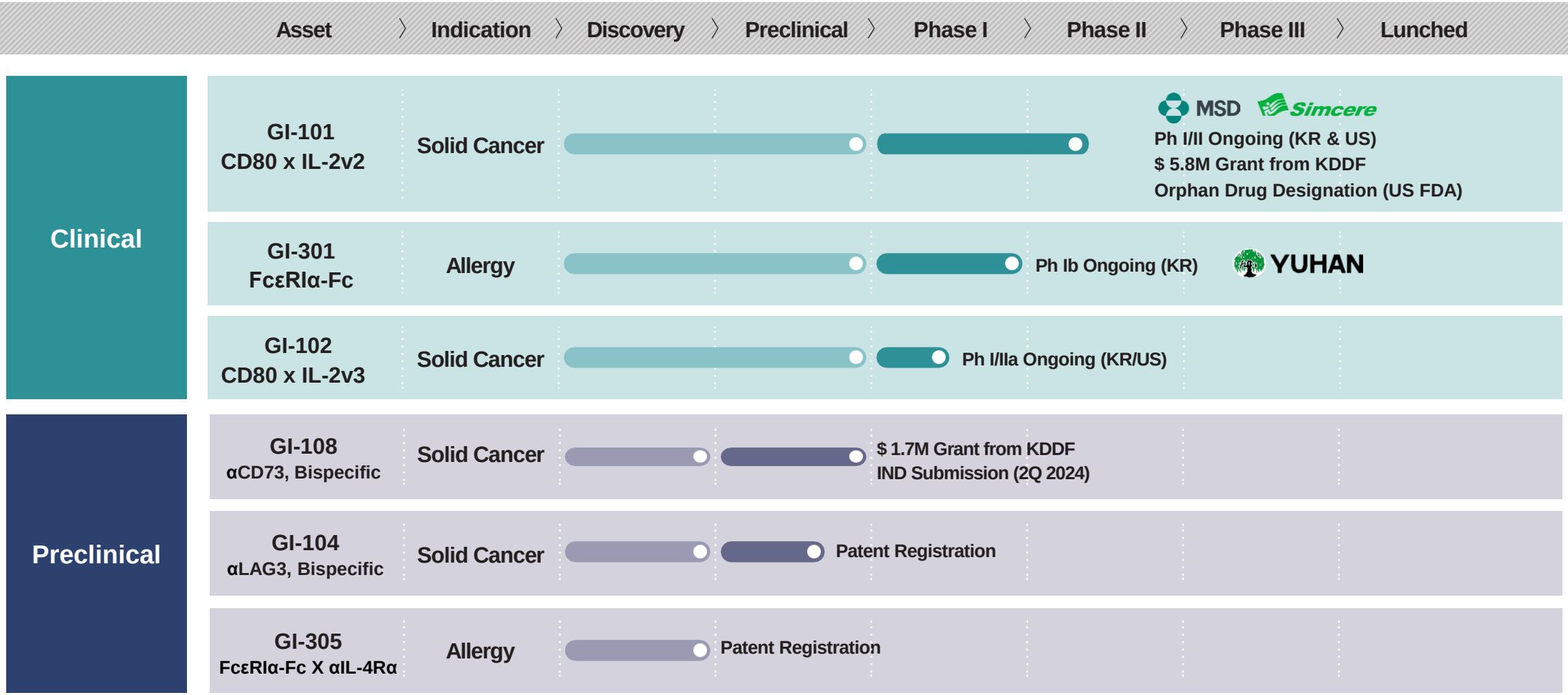


SMART-cLego™

Fast cloning by Lego-like block integration into an
Expression vector to save cost and time of protein production



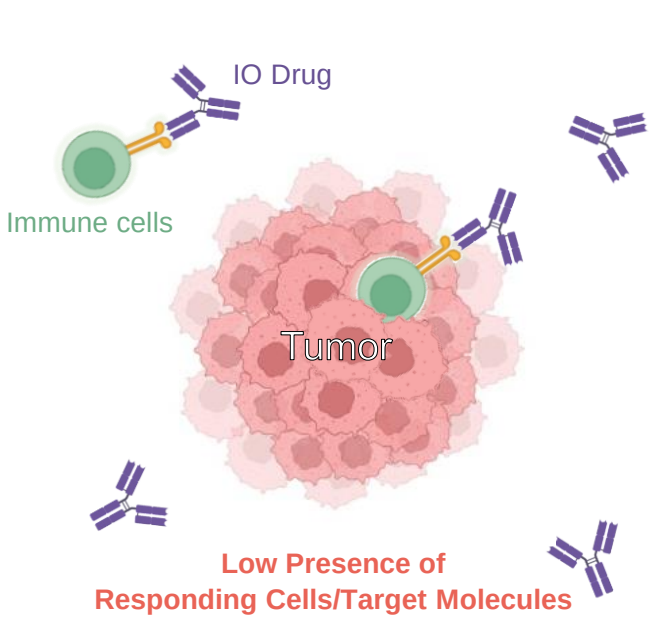
Pipeline


Asset
Indication
Discovery
Preclinical
Phase I
Phase II
Phase III
Lunched
Clinical
GI-101
CD80 x IL-2v2
Solid Cancer
MSD
Simcere
Ph I/II Ongoing (KR & US)
$ 5.8M Grant from KDDF
Orphan Drug Designation (US FDA)
GI-301
FcεRIα-Fc
Allergy
Ph Ib Ongoing (KR)
YUHAN
GI-102
CD80 x IL-2v3
Solid Cancer
Ph I/IIa Ongoing (KR/US)
Preclinical
GI-108
αCD73, Bispecific
Solid Cancer
$ 1.7M Grant from KDDF
IND Submission (2Q 2024)
GI-104
αLAG3, Bispecific
Solid Cancer
Patent Registration
GI-305
FcεRIα-Fc X αIL-4Rα
Allergy
Patent Registration

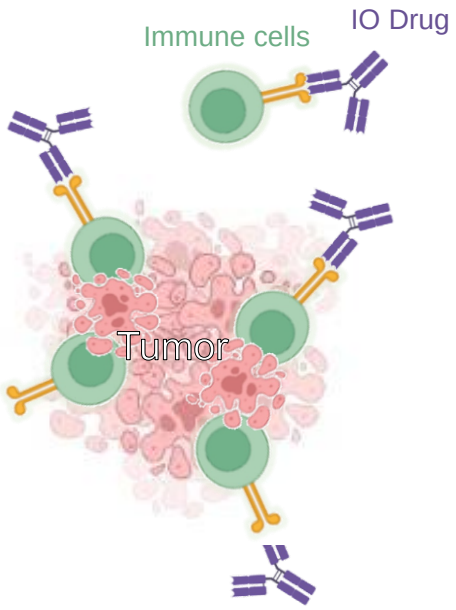
Innovative Immunokine ‘GI-101’

Unmet Needs in Checkpoint Blockade Therapy

Insufficient Immune Cells Leads to Ineffective Treatment



IO Treatment is Less Effective



IO Treatment is More Effective

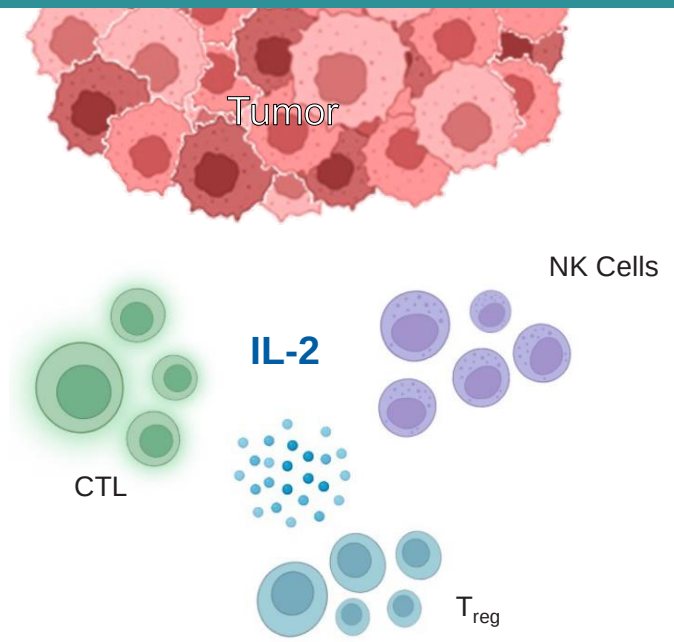
IL-2 increases the number and activity of the immune cells

Source: Dielhl et al., Oncotarget, 2017

Limitations in the Clinical Use of IL-2

IL-2 has strong anti-cancer activity but clinical use is limited due to safety concern

Induces the Expansion of CTL and NK Cells Along with T_{reg} Cells



Increase in Anti-Tumor Response

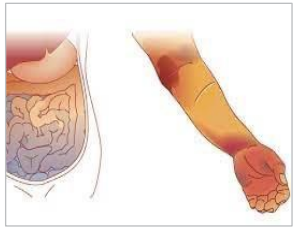
Cytotoxic T Lymphocyte and NK Cell Expansion

T_{reg} Expansion

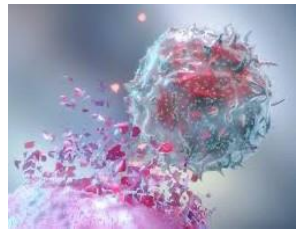
Suppression of Anti-Tumor Response

Safety Issue

Risk of VLS and CRS hinders sufficient dosing of IL-2 needed for the induction optimal Anti-tumor response

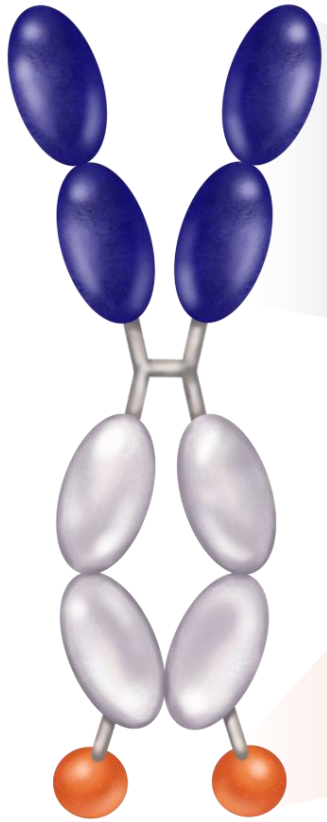


Vascular Leakage Syndrome



Cytokine Release Syndrome

GI-101, Synergetic Combination of CD80 and IL-2 for Enhance Efficacy

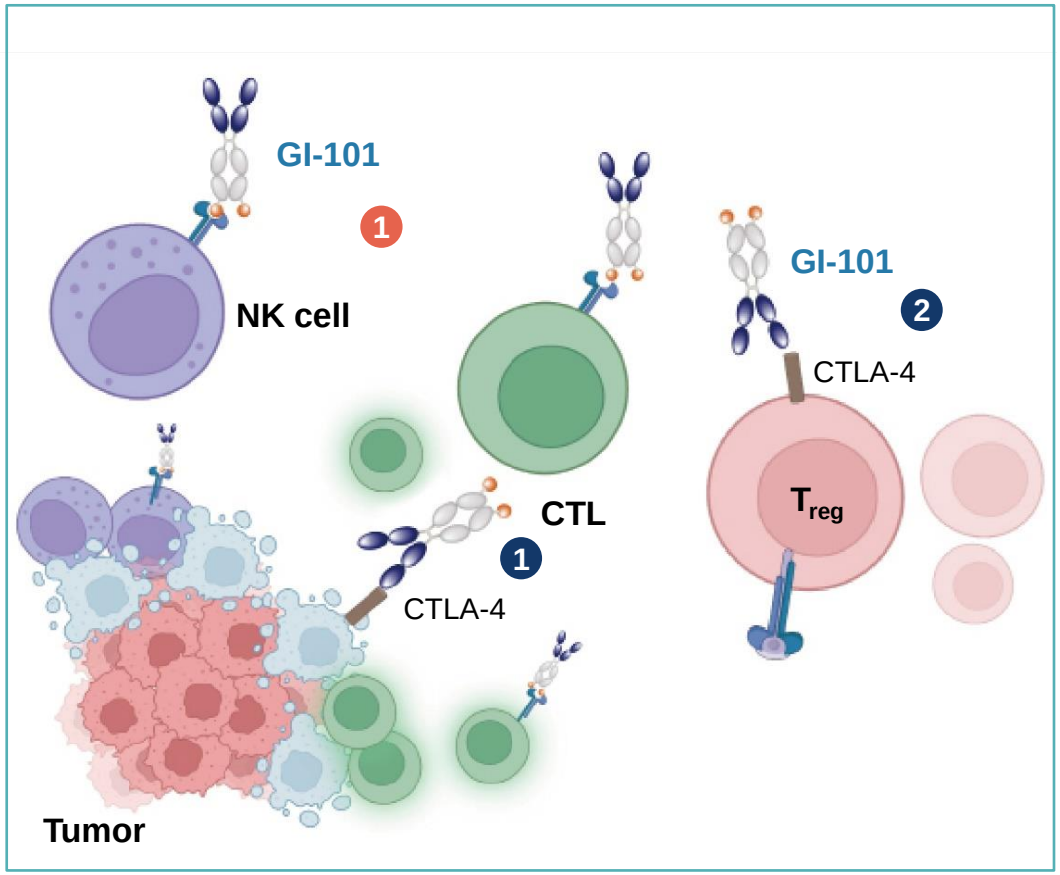


CD80

1. **Targeted Delivery to Tumor Site**
2. **Decrease T_{reg}-Mediated Immunosuppression by Blocking CTLA-4**

IL-2v2

1. **Strong Proliferation & Activation of Immune Cells**
   - **2 Amino Acid Variant**
     → Reduced IL-2Rα binding



CTL : Cytotoxic T Lymphocyte

Superior to Competitive Product and Pipeline

Category	Function	GI Innovation GI-101 (CD80 x IL-2v)	Bristol Myers Squibb Yervoy® (anti-CTLA4 Ab) CD80 Competitive	Bristol Myers Squibb Bempegaldesleukin (PEG-IL-2) IL-2 Competitive	Alkermes Nemvaleukin (Modified IL-2) IL-2 Competitive
Efficacy	CD8 T^+ Cell Proliferation	●	◑	◑	●
	NK cell Proliferation	●	N/A	●	●
	T_{reg} Cell Inhibition	●	●	○	○
Action	Targeting of Tumor and immune cells	●	●	N/A	N/A
Safety	Tolerability	●	○	○	○

●: High ◑: Intermediate ○: Low

Source: modified from Sanofi R&D Investor Event, June 23,2020 / Sanofi Oncology ASCO Event, June 4, 2021 /. Alkermes corporate presentation

Superior Safety over Proleukin® & Competitive IL-2 Agents

Recommended Phase 2 Dose was set at 0.3 mg/kg: 10-fold higher IL-2 amount vs non-alpha IL-2 agents

	GI-101 monotherapy (N=57)	Proleukin® (N=270)*
≥ Grade 3 ADR	**11 (19%)**	**257 (95%)†**
≥ Grade 4 ADR	**0 (0%)**	**95 (35%) †**
ADR leading to death	**0 (0%)**	**6 (2%)**
Most common ADR (>20%)	Fever (67%), increased AST (21%)	Hypotension (64%), vomiting (55%), diarrhea (54%), bilirubin elevation(51%), hypouresis (49%), fever (47%), thrombocytopenia (43%), Increased aminotransferase (39%), Increased blood creatinine (35%), malaise (34%), difficulty in breathing (31%), chaos (30%), anemia (29%), rash (27%), nausea (24%), leucopenia (21%)

ADR: Adverse Drug Reaction
* Patients with Metastatic Melanoma (analysis of 270 patients treated between 1985 and 1993)
** Grade 4 Lymphopenia
† Oncology News International vol 7 No 2 CancerNetwork Feb 1998

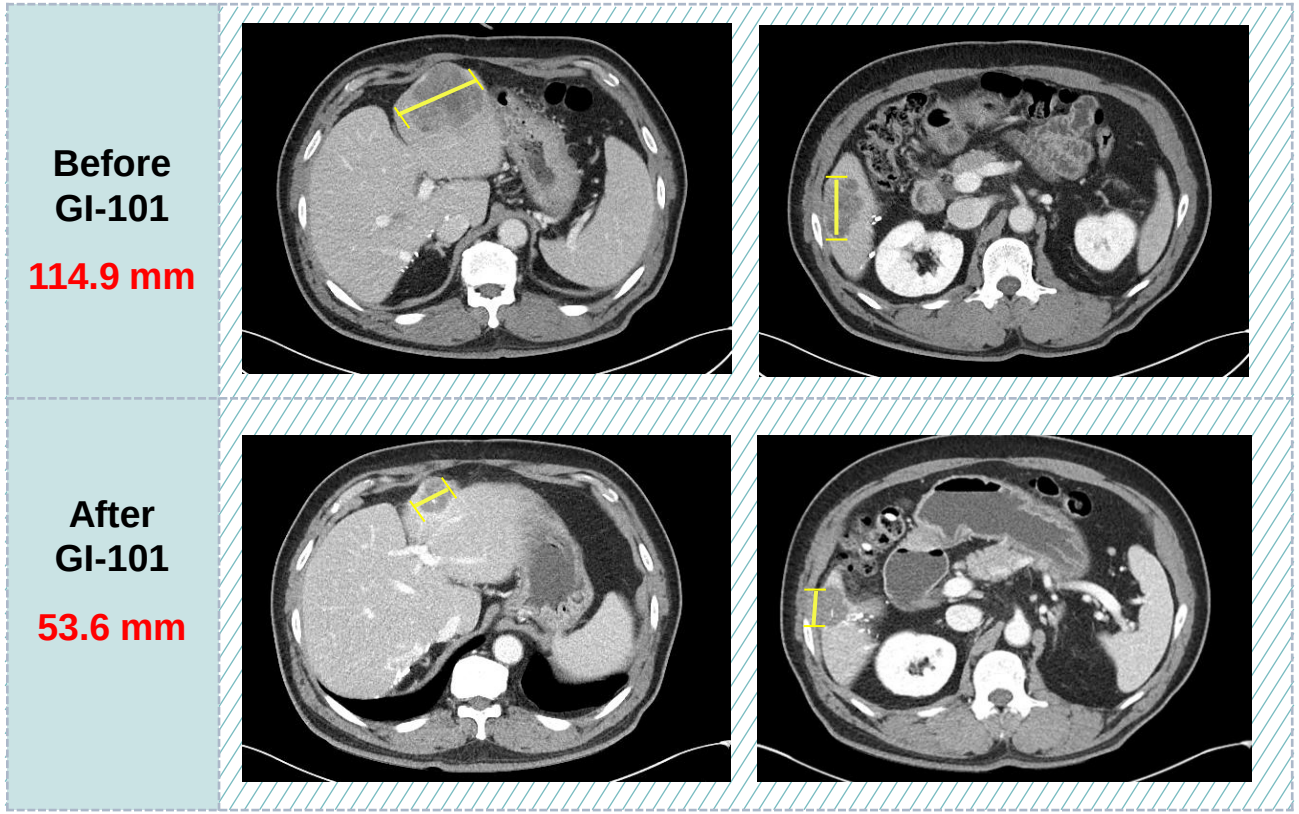
GI-101 Monotherapy Shows Promising Anti-Cancer Activity (1/2)

In monotherapy dose escalation and expansion phase:
1 CR, 3 PRs and 1 SD over 6 months in patients with solid tumor who failed on SoC

Case #1: MSS Colorectal Cancer

MSS Colorectal Cancer with Liver Metz

GI-101	0.018 mg/kg
Prior line of therapy	3rd line
Objective response	**SD (reduction of target lesion -53.57%)**
Treatment period	Ongoing **(1.5 + year)**



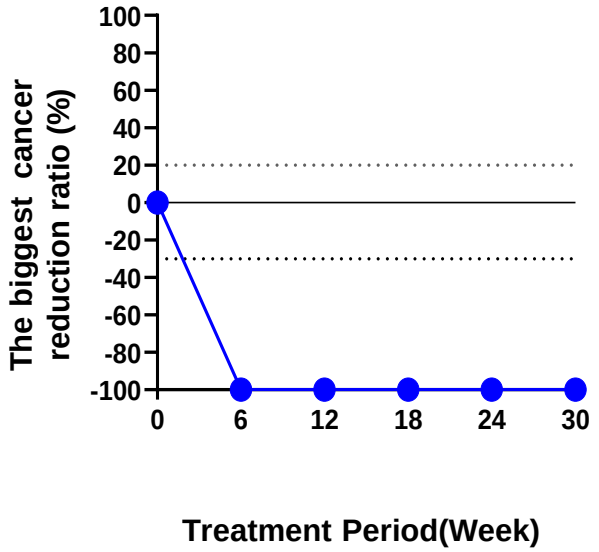
GI-101 Monotherapy Shows Promising Anti-Cancer Activity (2/2)

In monotherapy dose escalation and expansion phase:
1 CR, 3 PRs and 1 SD over 6 months in patients with solid tumor who failed on SoC

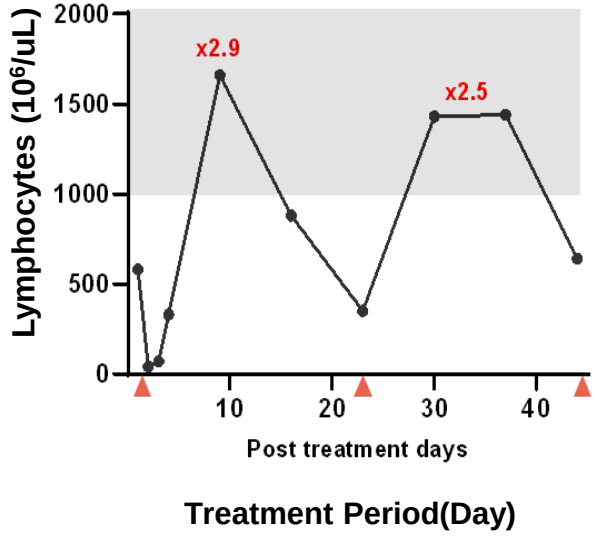
Case #2: pMMR Cervical Cancer

pMMR Cervical Cancer	
GI-101	0.3 mg/kg
Prior lines of therapy	2nd line
Objective response	**CR (reduction of target lesion -100%)**
Treatment period	Ongoing **(7 month)**

CR after 2 cycles of GI-101
DoR 5+ months

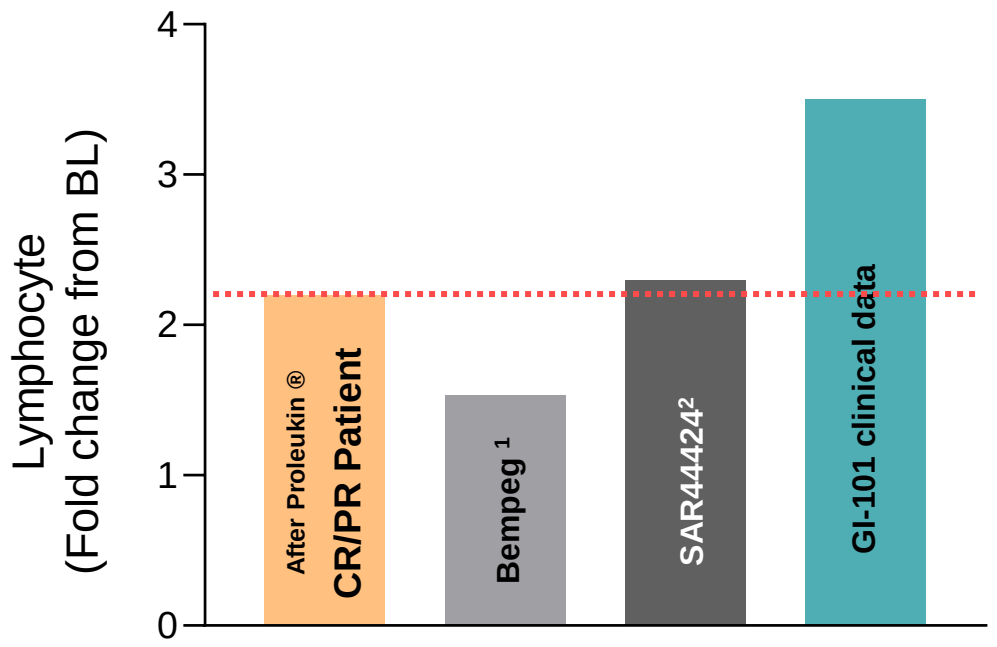


Overcoming lymphopenia by GI-101

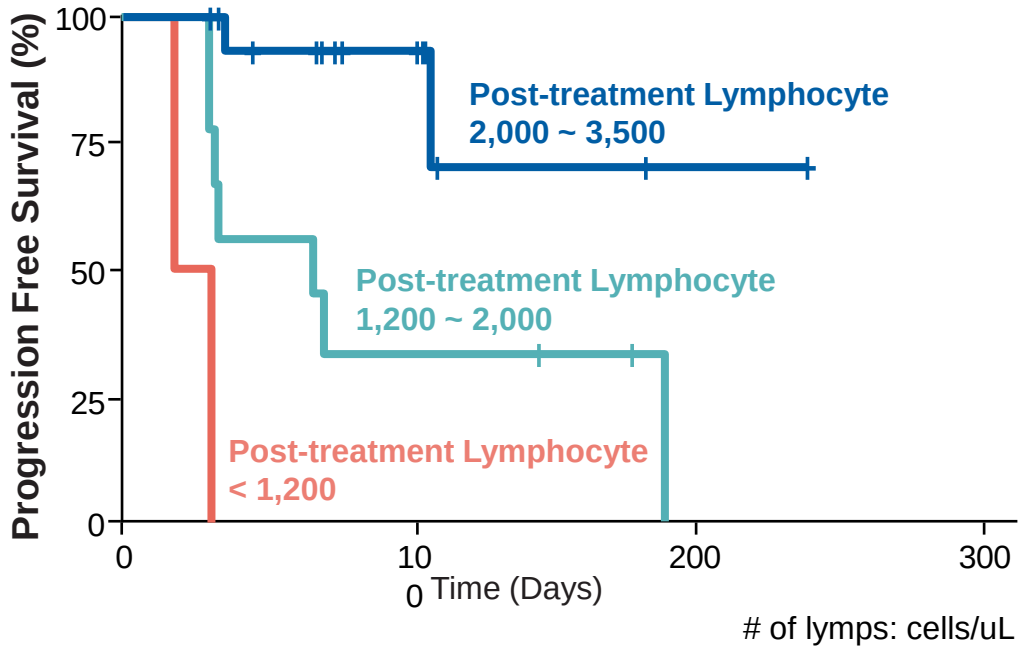


Lymphocyte Expansion Correlates with Anti-Cancer Activity of GI-101

Lymphocyte expansion after IL-2 treatment

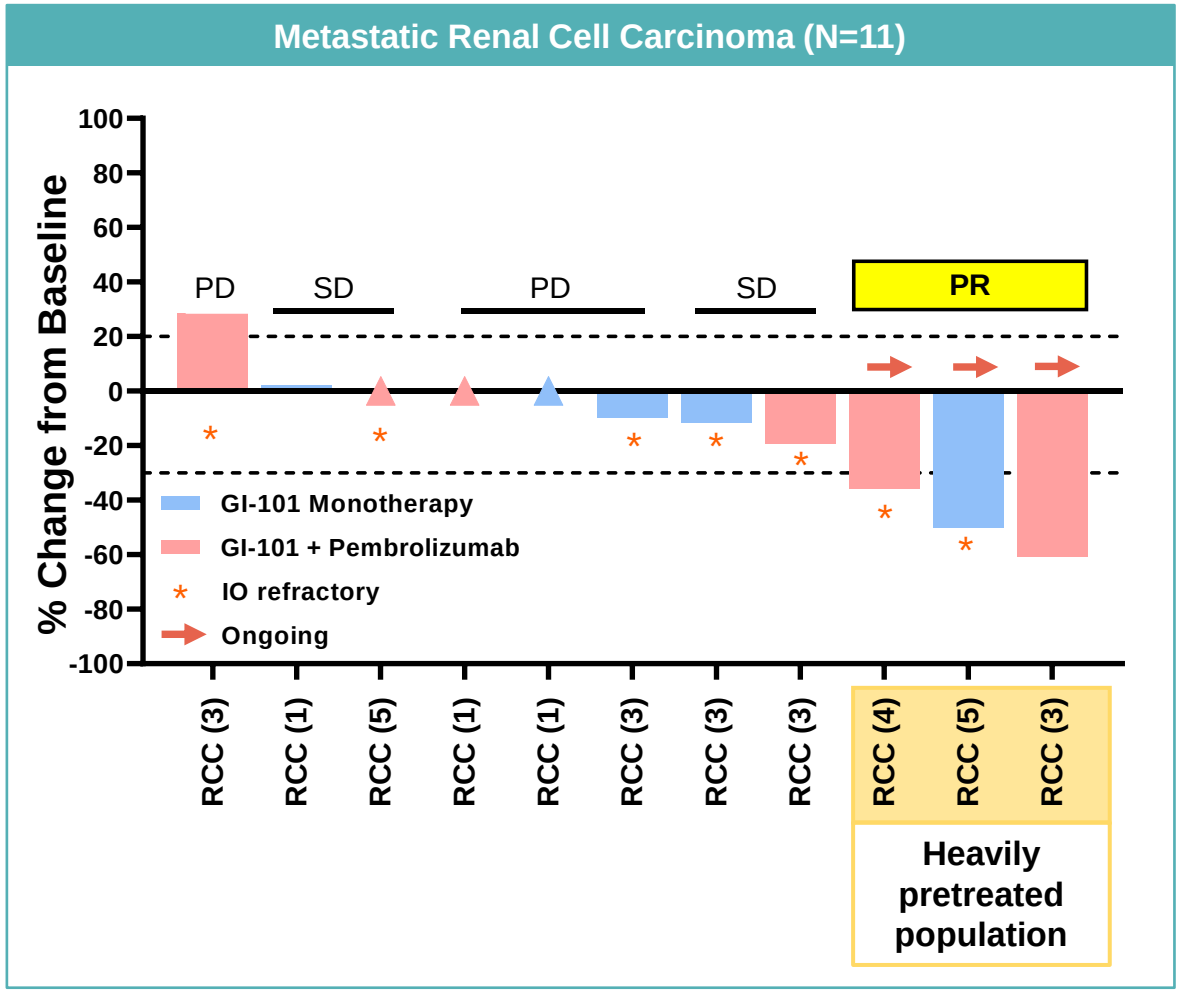


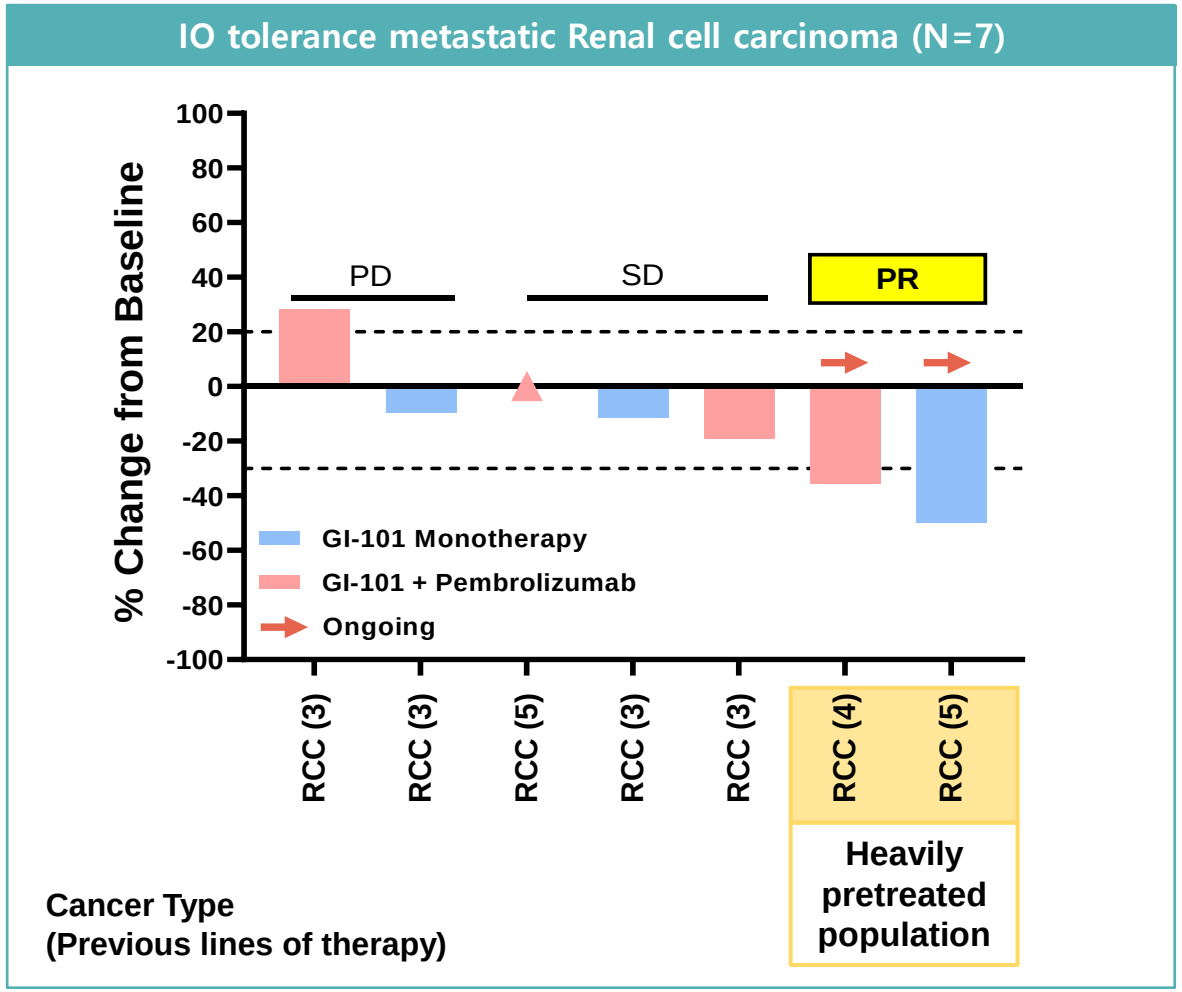
PFS after GI-101 Monotherapy (Clinical Data)



1. Nektar Therapeutics., ASCO Presentation. 2017
2. Sanofi 2020 R&D presentation

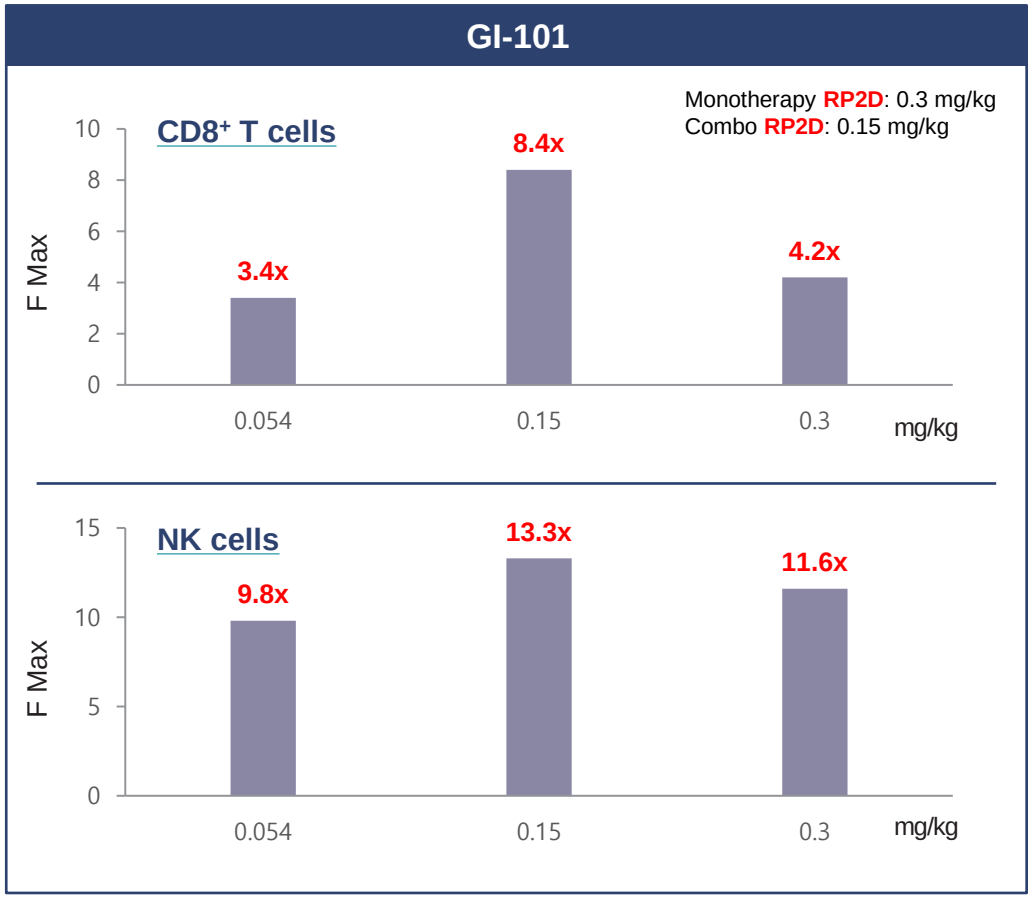
GI-101 has potential to overcome CPI resistance

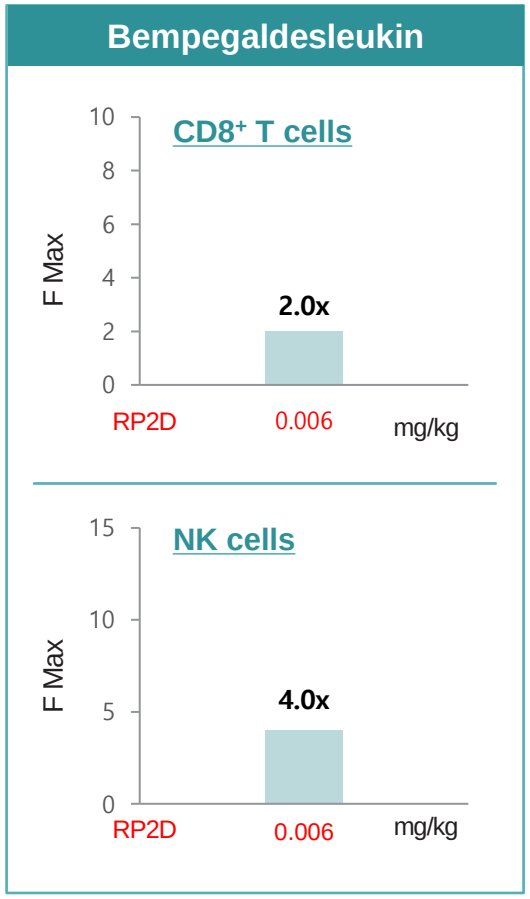


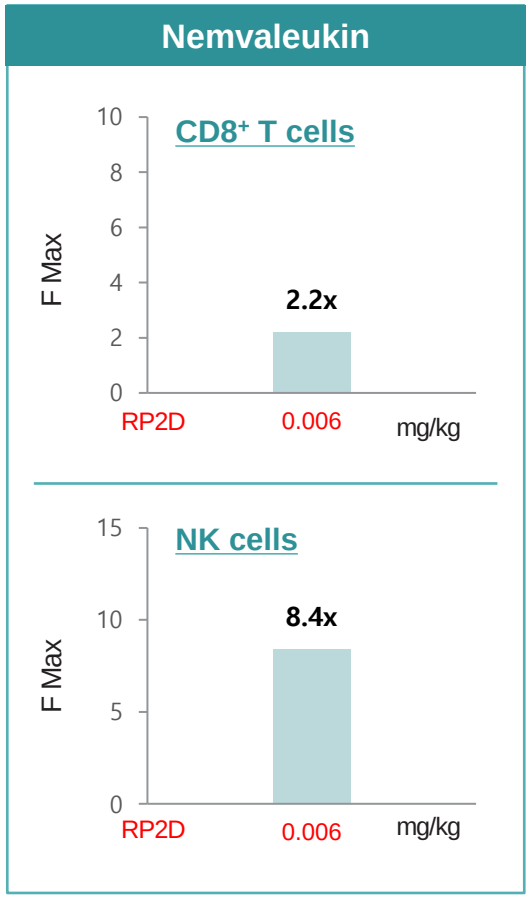


%Change from BL until PD per RECIST v1.1; Data cut-off 06 Jul 2023

GI-101 Induces Robust Proliferation of Effector Cells





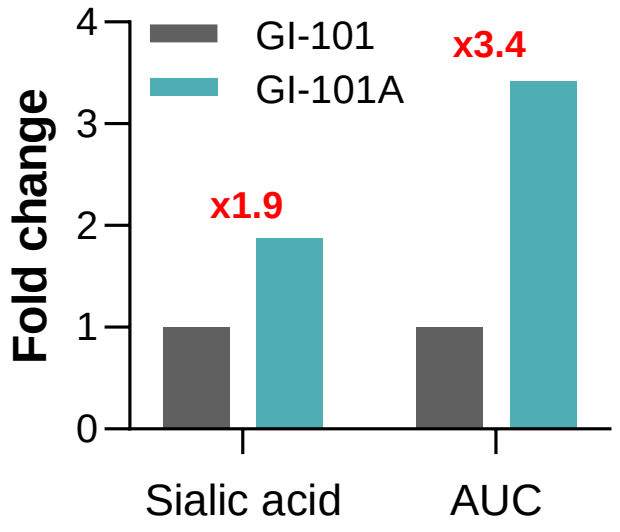


Data cut-off: 27 Dec 2022; Alkermes corporate presentation, Sanofi corporate presentation

GI-101A: GI-101 with High Sialic Acid

Formulation Improvement

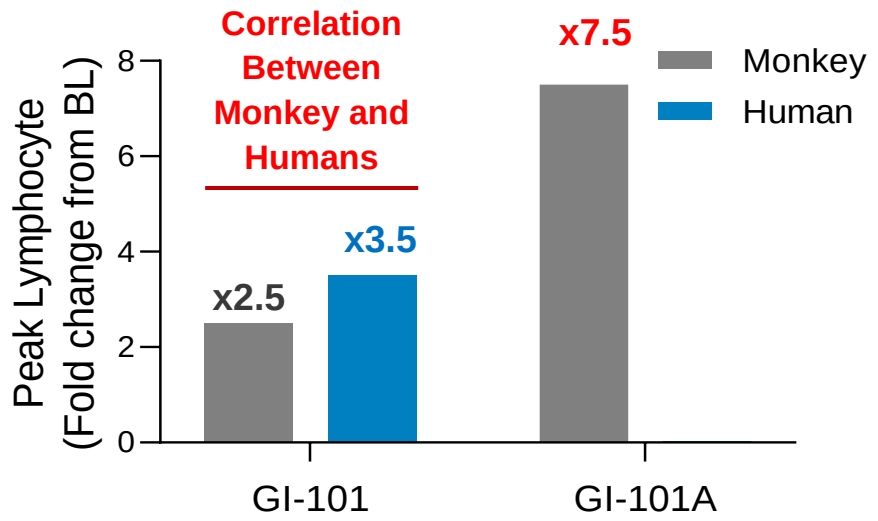
Improved manufacturing process developed by SAMSUNG BIOLOGICS



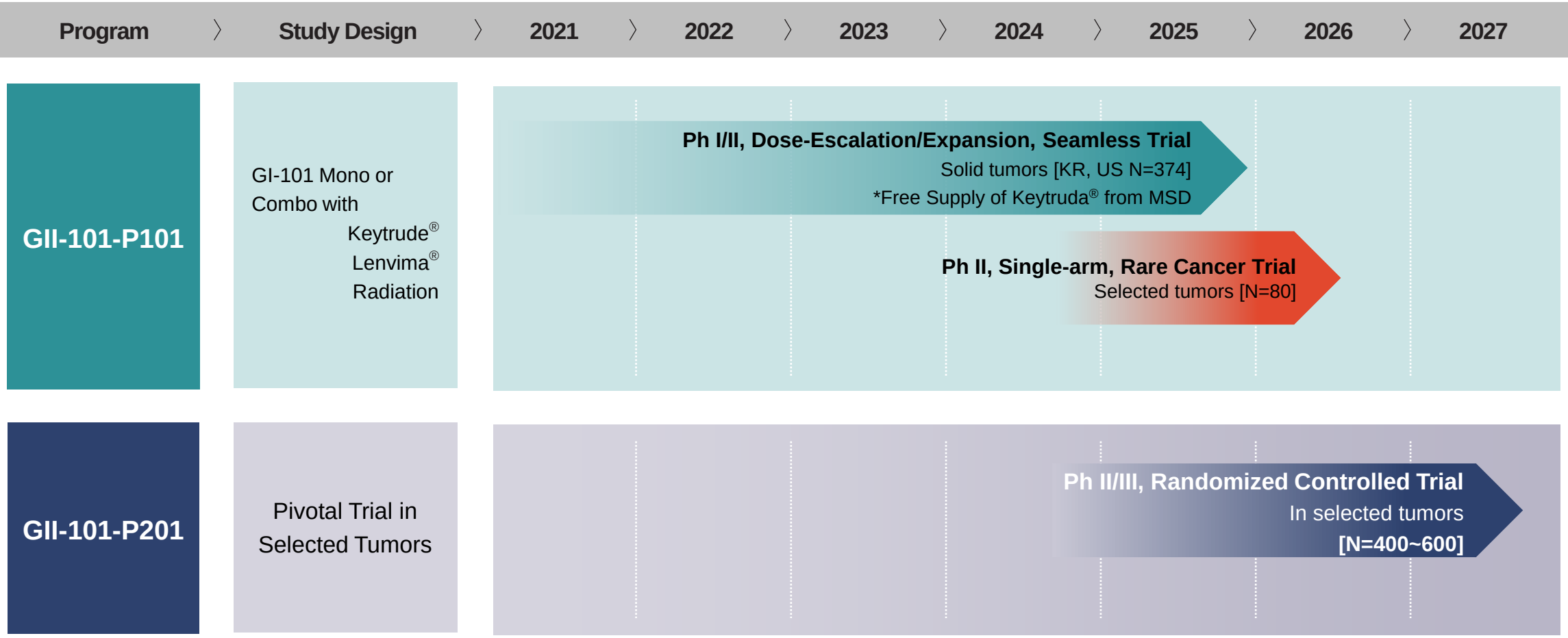
Manufacturing robustness enabling early commercialization

Improved PD profile vs GI-101

Based on the monkey data, significant lymphocyte expansion is expected with GI-101A



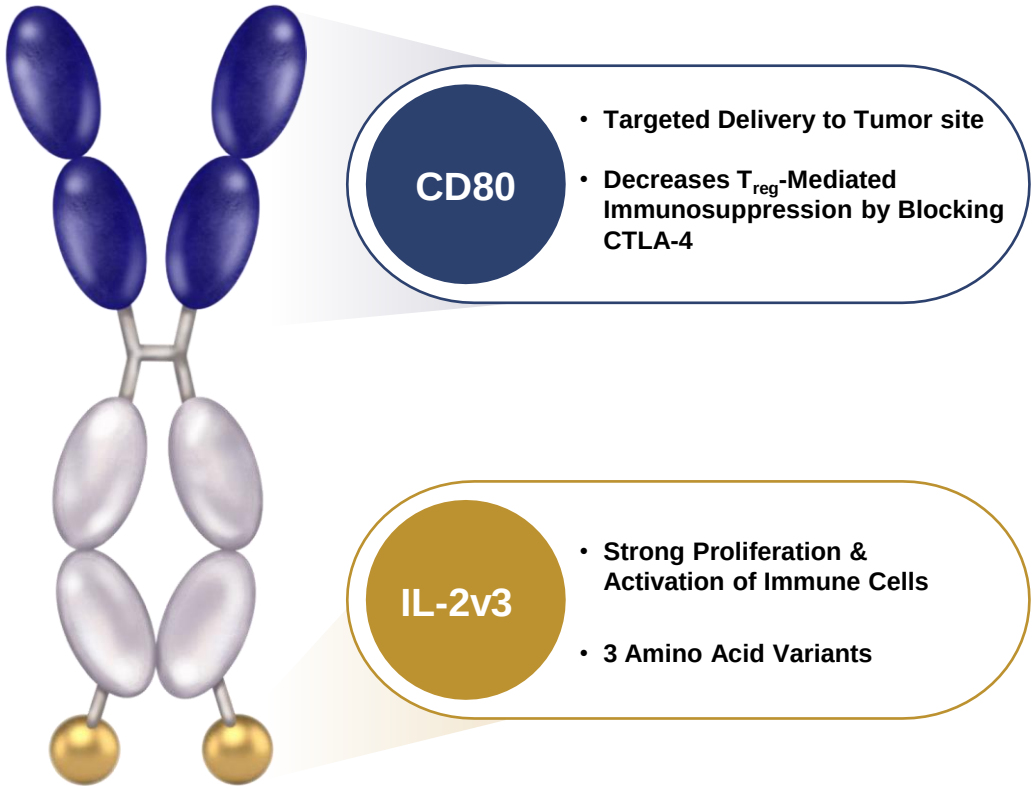
Clinical Development Plan of GI-101



Game Changing Next-Generation Immunokine ‘GI-102’

GI-102, Super Immunokine with the Advantage of SC Delivery

Bispecific Design



CD80

- **Targeted Delivery to Tumor site**
- **Decreases T_{reg}-Mediated Immunosuppression by Blocking CTLA-4**

IL-2v3

- **Strong Proliferation & Activation of Immune Cells**
- **3 Amino Acid Variants**

Competitive Advantage

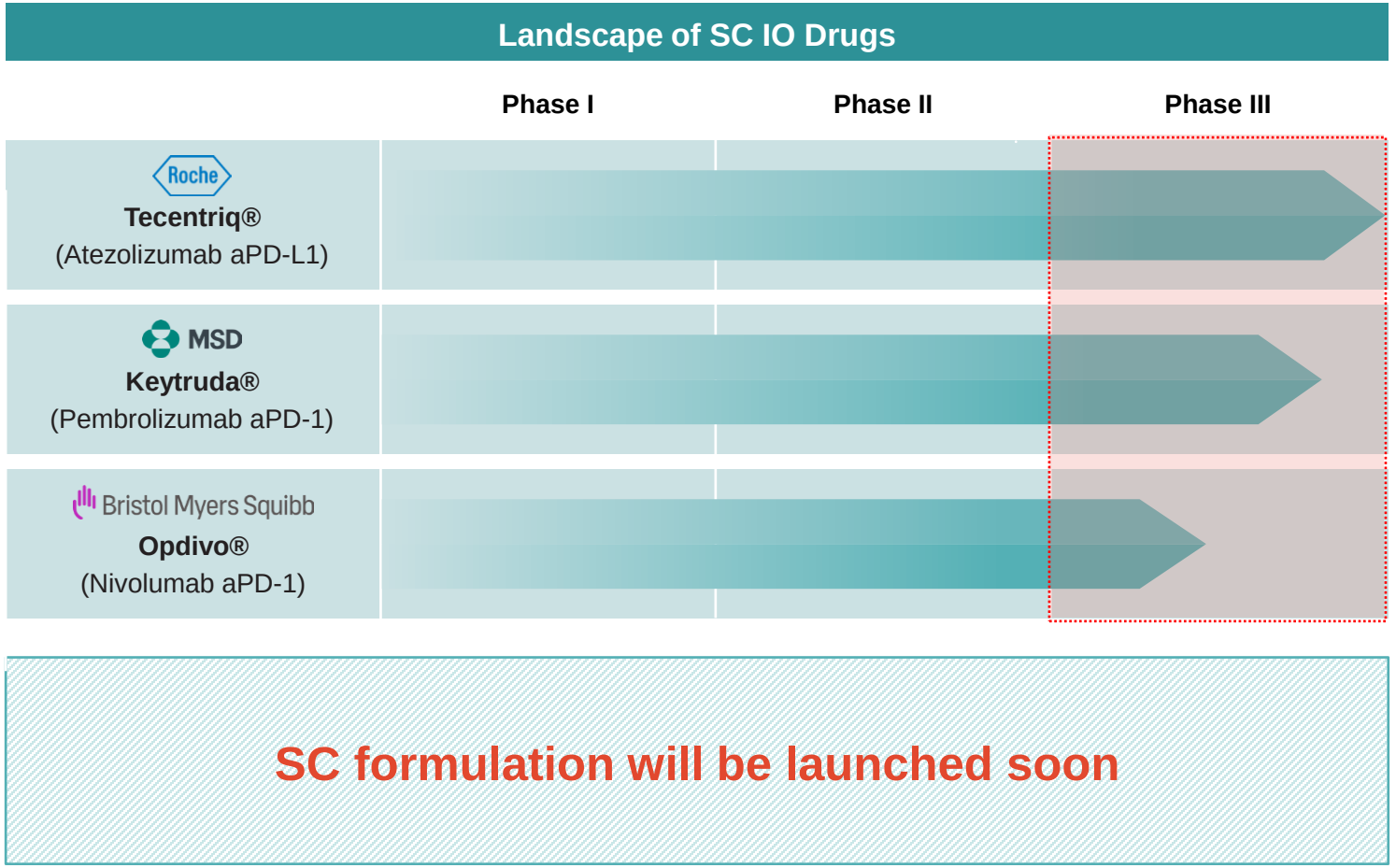
High Anti-Tumor Activity

Simultaneously increases the number and the activity of cytotoxic T lymphocytes and NK cells

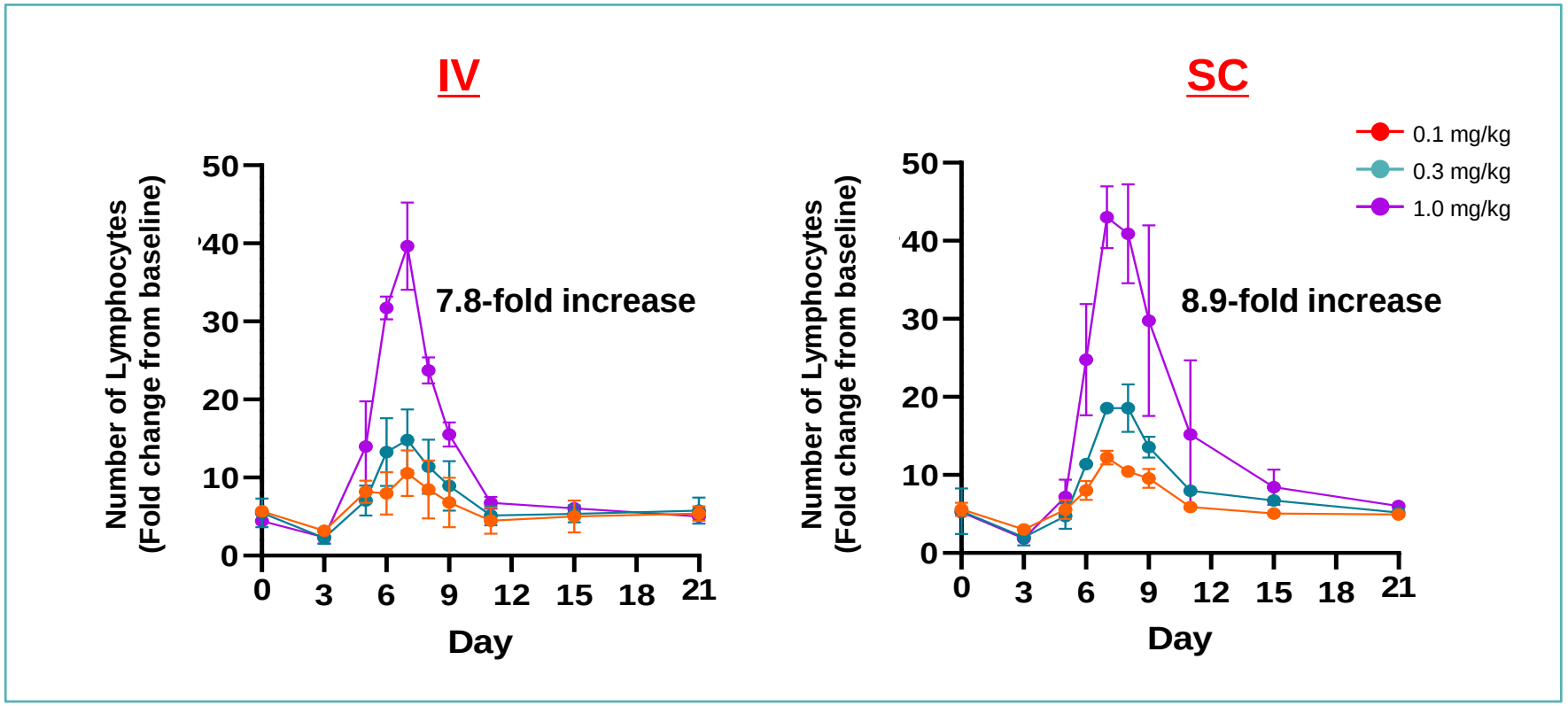
SC Delivery

High content of sialic acid allows SC delivery without changing the formulation

SC Delivery as a Global Trend in Immuno-Oncology



Immune Cell Expansion Between IV and SC Administration in Monkeys

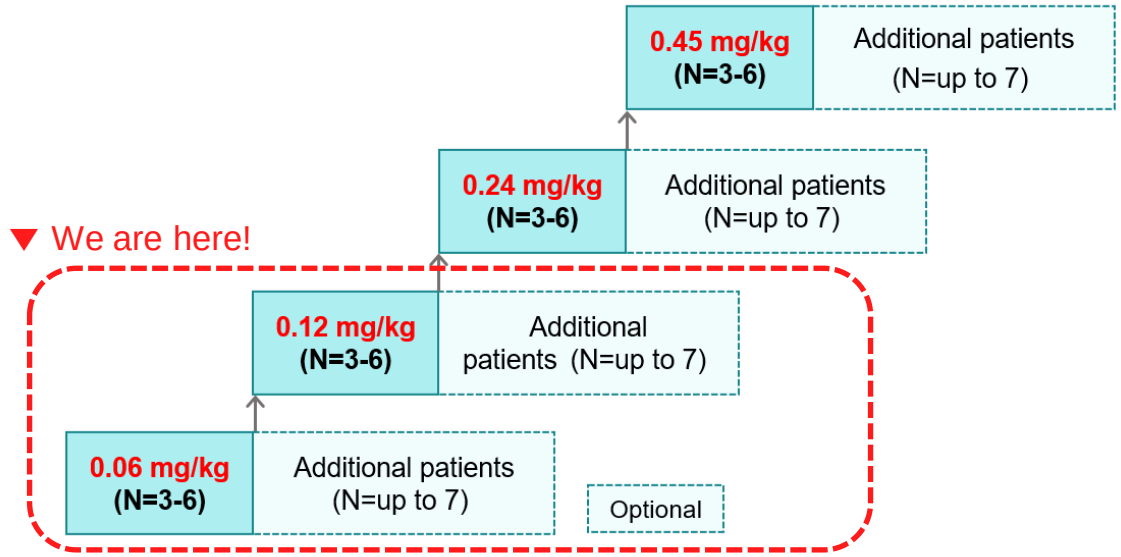


GI-102 Study Design

Study is undergoing in Korea and US

Dose escalation phase (3+3 design) in all comers
(Total N=approx. 52)

GI-102: mg/kg, IV, Q3W



- In dose escalation, enrollment in each cohort may be extended, potentially enriched in certain tumor types and/or characteristics to confirm totality of clinical data, if applicable **(N=up to 7/cohort)**
- **Additional patients enrolled in each dose escalation cohort are not subject for DLT evaluation and baseline and on-treatment biopsies are mandated**

Dose expansion phase
(Total N=approx. 40)

GI-102: mg/kg, IV, Q3W

Tentative RP2D

Solid cancers failed on available SOC (N=40)

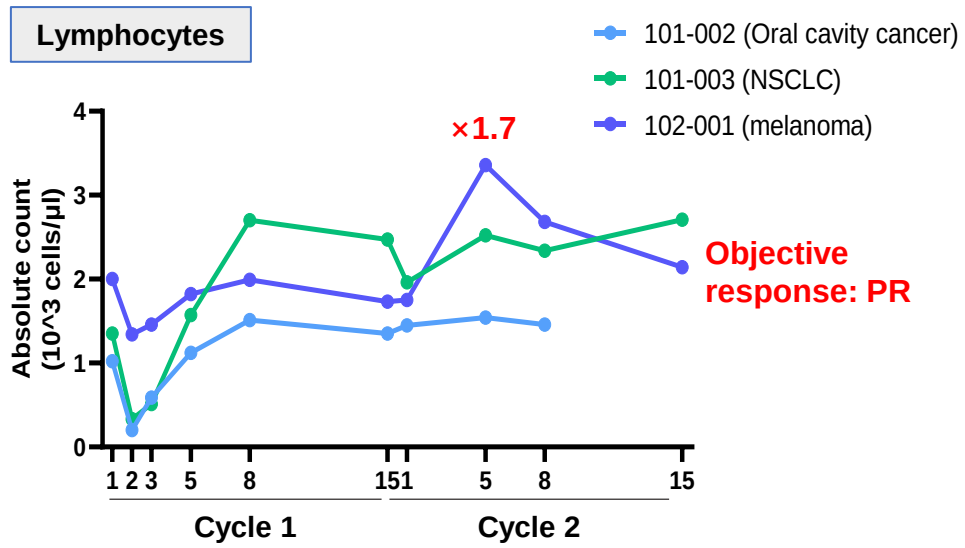
RCC (n=10), Melanoma (n=10)

- Tentative RP2D will be optimized through 1:1 randomization. The protocol will be amended accordingly.
- In dose expansion phase, **If ORR exceeds 10% in the certain tumor types,** the enrollment of the that tumor type can be expanded to have up to 20 response-evaluable patients

Abbreviation: RP2D= Recommended phase 2 dose; RCC=Renal cell cancer

GI-102 is Showing Early Clinical Signal

GI-102 0.06 mg/kg

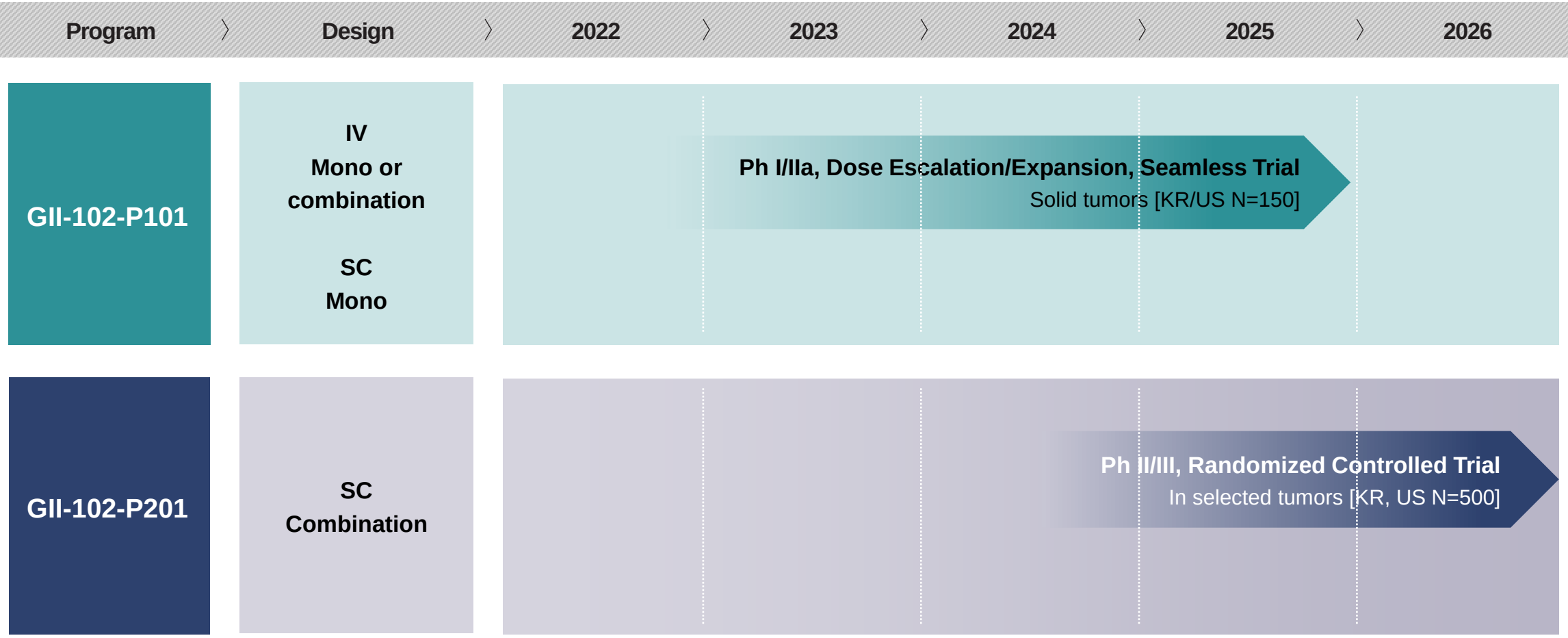


- Among 3 patients dosed GI-102 0.006 mg/kg, **1 patient (Melanoma) had uPR (Partial Response)** after 2 cycles of GI-102 (based on RECIST v1.1)

[Patient demography]

- Stage II Melanoma, Female, 70 years
- Initial diagnosis: Apr 2012
- Treatment history
  - 1L Pembrolizumab (2017-2019)
  - 2L Cisplatin + Dacarbazine + Tamoxifen (2019-2020)
  - 3L ATR kinase inhibitor + Durvalumab (2020-2021)

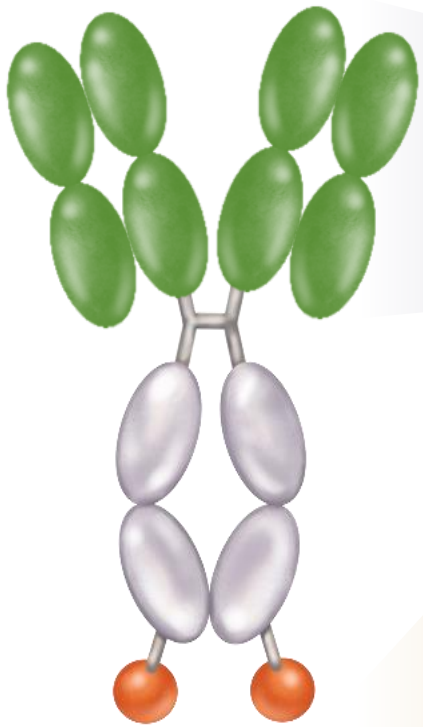
Clinical Development Plan of GI-102



Bispecific to overcome immune resistance: ‘GI-108’

GI-108, Dual-targeting action via anti-CD73 and undisclosed target

Bispecific Design



α-CD73

- Targeting of CD73 overexpressing tumor cells
- Inhibits AMP breakdown to adenosine
- Designed to remediates immune system from tumor-mediated immunosuppression

Undis-closed

- Strong Proliferation & Activation of Immune Cells

Competitive Advantage

High Anti-Tumor Activity

Low efficacy with other targets in adenosine pathway (CD39, A2AR)

No clinical benefit with current CD73 monotherapy

Bispecifics or combination therapy is needed

IND Submission planned in Korea: 2024' 2Q

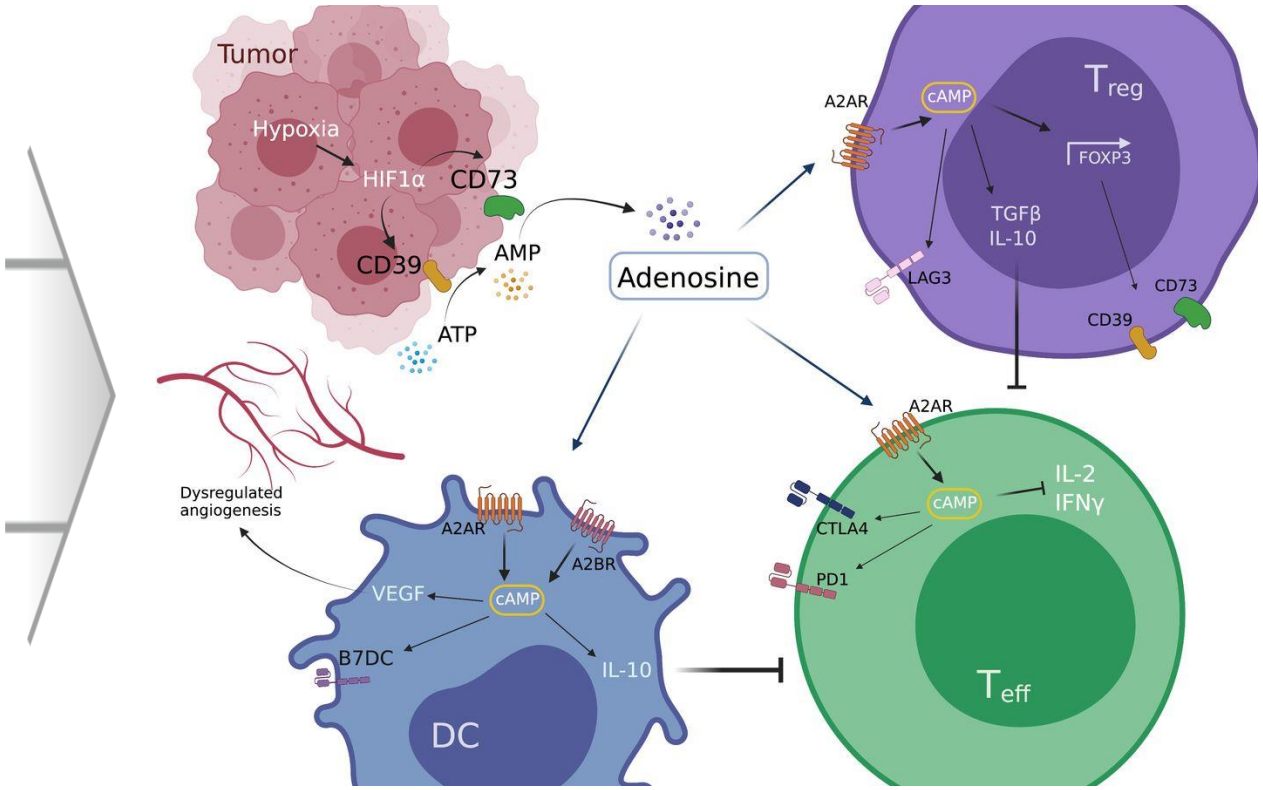
CD73 is critical for immune resistance

Blocking CD73

- **Overcomes immune suppression in adenosine-enriched tumors**
- **Reinvigorates immune response**

Combining IL-2

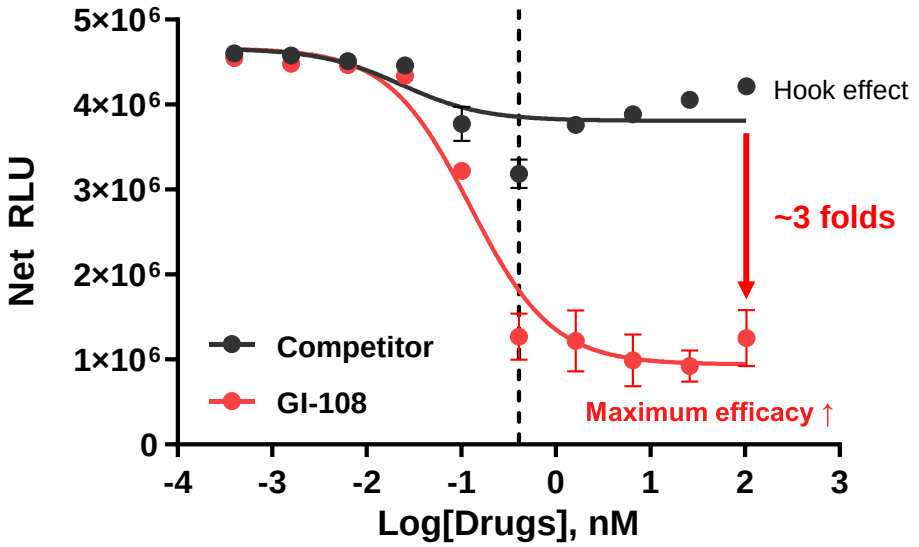
- **Synergizes to induce strong proliferation/activation of effector T and NK cells**



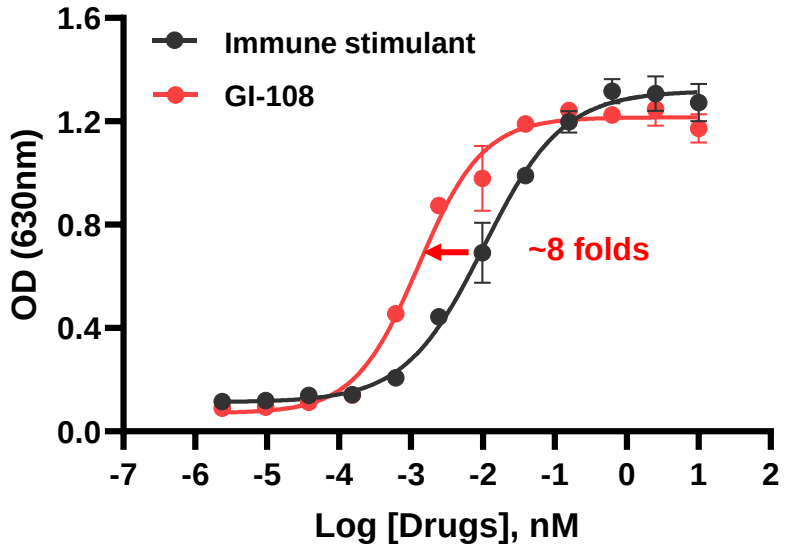
Modified from: 1. Augustin RC et al., JITC. 2022; 2. Masso-Silva JA et al., Front Immunol, 2022;
3. Horvath L et al., Mol Cancer, 2020; 4. Stultz J et al., Prostate Cancer, 202; 5. Petrova et al., IJMS, 2020;

GI-108 Shows Promising Efficacy Compared to Competitor Programs

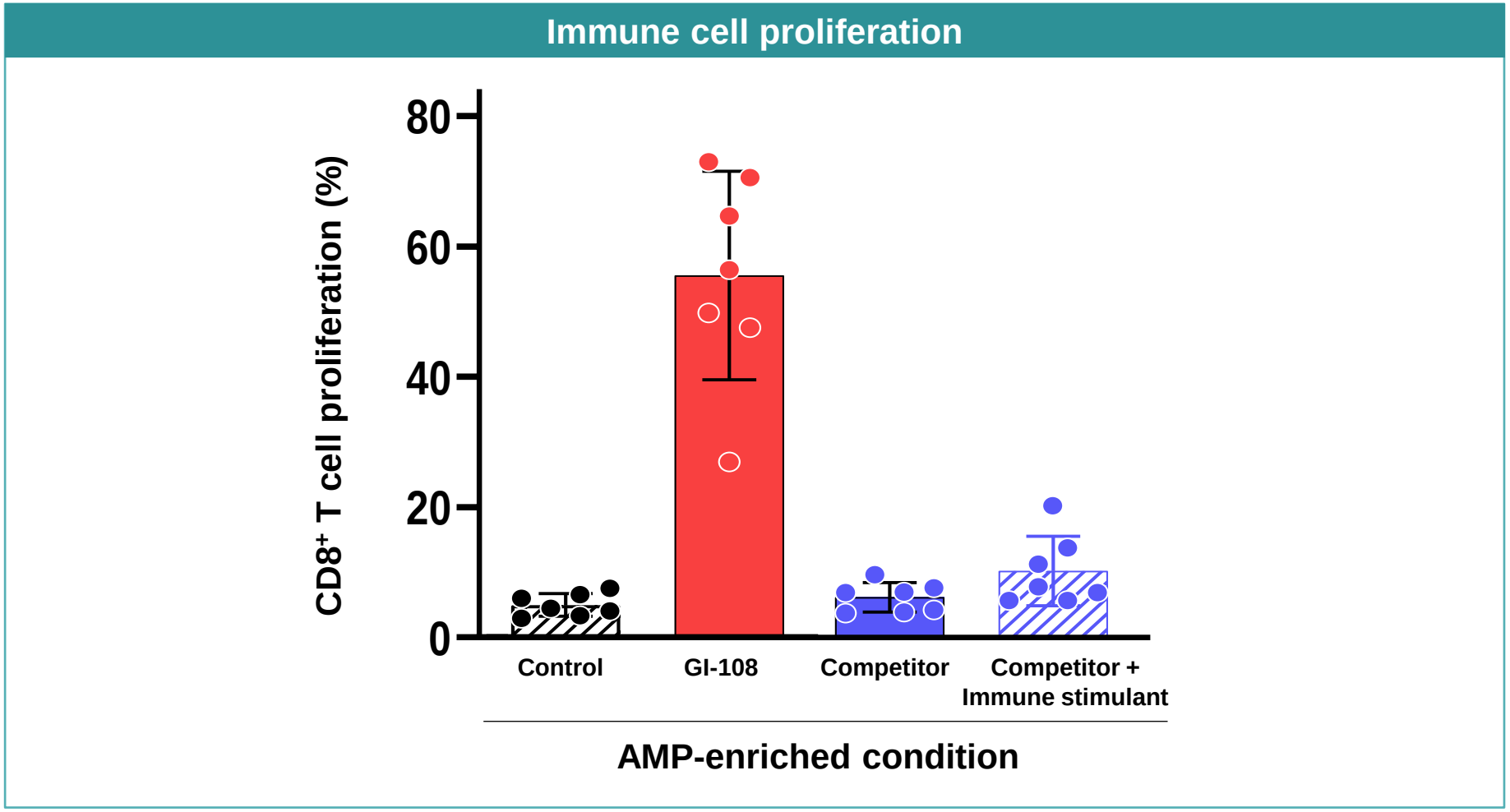
CD73 enzyme activity



Immune cell activation signaling

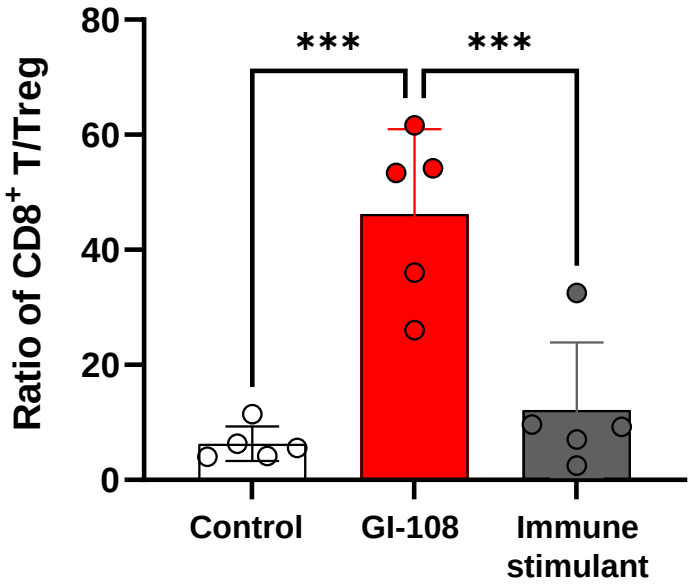


GI-108 Induces CD8 T Cell Proliferation in AMP-Enriched Condition

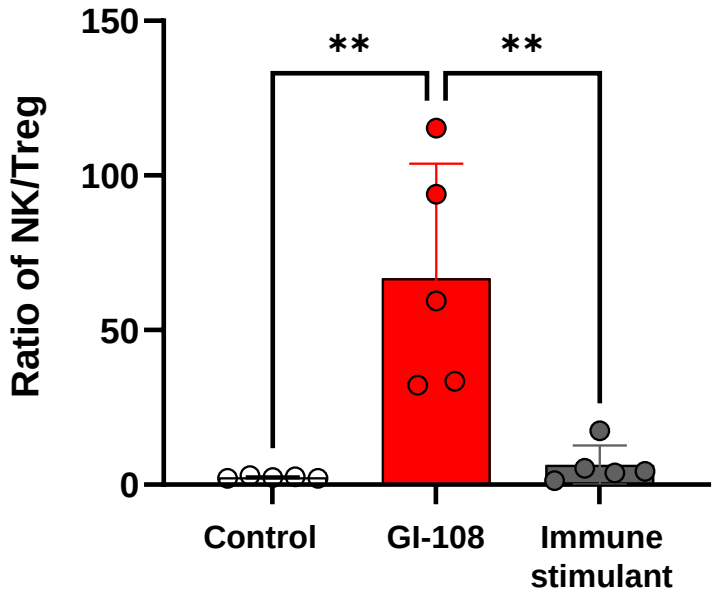


GI-108 Induces Significant Changes in Immune Cell Composition in Tumor Microenvironment

$CD8^+$ T / Treg Ratio (TME)



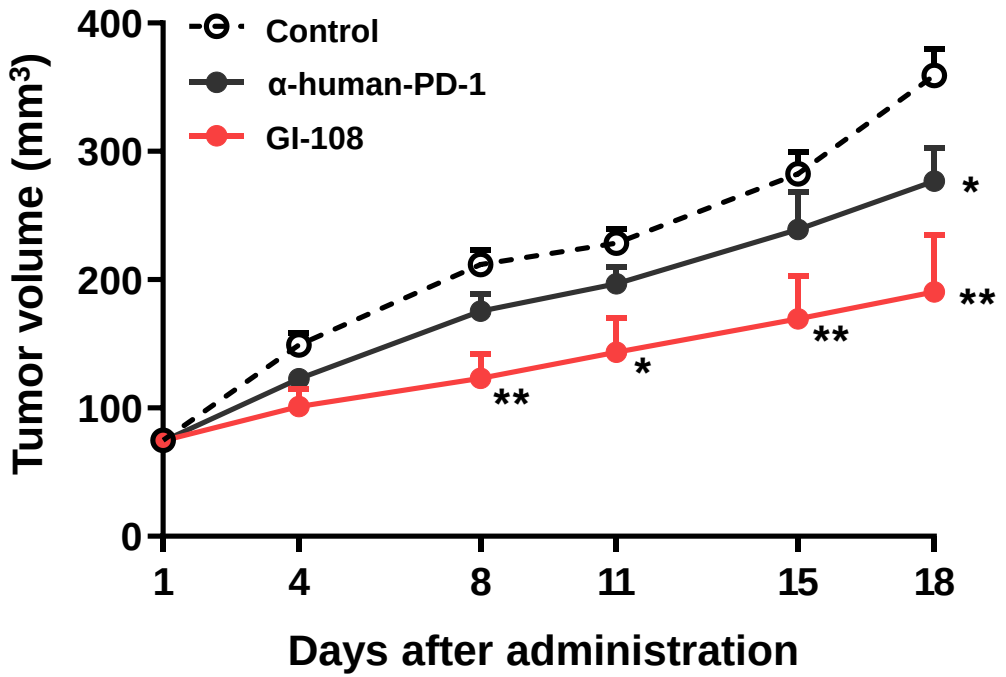
NK / Treg Ratio (TME)



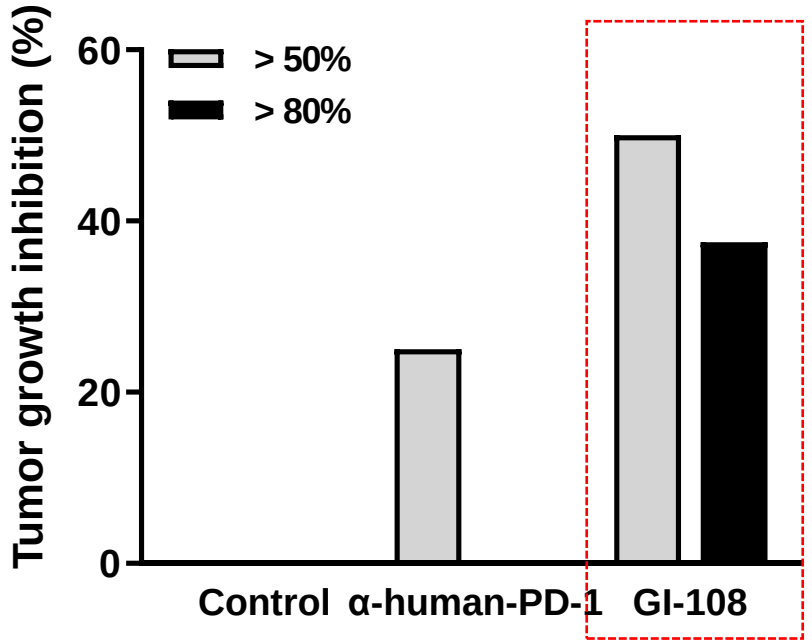
GI-108 elicits anti-tumor effect in humanized mice

Anti-tumor response was evaluated in humanized mouse model (MHC class I–null B2M NSG) after human PBMC transplantation, grafted with **MDA-MB-231, triple-negative breast cancer cell line, having high PD-L1 and CD73 expression**

Tumor Volume



Tumor Growth Inhibition



Clinical Development Plan of GI-108

Targets CD73 expressing tumor with high unmet medical needs, e.g., Pancreatic cancer