# INVESTOR PRESENTATION

March 2024

# Forward-Looking Statements

Certain statements set forth in this presentation constitute “forward-looking statements” within the meaning of the Private Securities Litigation Reform Act of 1995, as amended. The words “anticipate,” “believe,” “expect,” “may,” “will” and similar expressions are intended to identify forward-looking statements. Forward-looking statements made in this presentation include, but are not limited to, statements concerning: the protein engineering capabilities of Mural Oncology plc (the “Company”); the potential therapeutic and commercial value, and anticipated safety profile, of the Company’s engineered cytokine programs and product candidates, including nemvaleukin alfa (“nemvaleukin”) as a cancer immunotherapy when used as monotherapy or in combination, and its broad potential utility across a wide array of tumor types and indications and its potential dosing optionality; the Company’s expectations regarding timelines and plans for the development of its engineered cytokines, including, for nemvaleukin, expectations related to ongoing clinical studies in the ARTISTRY development program, the ability of ongoing studies to support potential registration, and potential for expansion of the development program, including to explore novel combinations with other cancer treatments; and the sufficiency of the Company’s existing cash resources for the period anticipated. You are cautioned that forward-looking statements are inherently uncertain. Although the Company believes that such statements are based on reasonable assumptions within the bounds of its knowledge of its business and operations, the forward-looking statements are neither promises nor guarantees and they are necessarily subject to a high degree of uncertainty and risk. Actual results may differ materially from those expressed or implied in the forward-looking statements due to various risks, assumptions and uncertainties. These risks, assumptions and uncertainties include, among others: the inherent risks and uncertainties associated with competitive developments, preclinical development, clinical trials, recruitment of patients, product development activities and regulatory approval requirements; preclinical or interim results and data from ongoing clinical studies of the Company’s cytokine programs and product candidates may not be predictive of future or final results from such studies, results of future clinical studies or real-world results; future clinical trials or future stages of ongoing clinical trials may not be initiated or completed on time or at all; the Company’s product candidates, including nemvaleukin, could be shown to be unsafe or ineffective; changes in the cost, scope and duration of development activities; the U.S. Food and Drug Administration (“FDA”) may make adverse decisions regarding the Company’s product candidates; the separation may adversely impact the Company’s ability to attract or retain key personnel that support the Company’s oncology business; and those risks, assumptions and uncertainties described under the heading “Risk Factors” in the Company’s filings with the Securities and Exchange Commission (“SEC”), including its Annual Report on Form 10-K for the fiscal year ended December 31, 2023, and in subsequent filings the Company may make with the SEC, which are available on the SEC’s website at www.sec.gov. Existing and prospective investors are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof. Except as required by law, the Company disclaims any intention or responsibility for updating or revising any forward-looking statements contained in this presentation.

SECTION 1:

# EXECUTIVE SUMMARY

# Mural Oncology

**Proprietary Cytokine Engineering Technology**
Proven to retain cytokine potency while overcoming limitations

Phase 2/3

**Late-Stage Clinical Biotech**
Lead asset (nemvaleukin) in two potentially registrational trials

**Well-Funded**
Cash runway into 4Q 2025

## Key Upcoming Catalysts

### 2024

✓ **1Q:** RP2D for next generation dosing schedule
**2Q:** Preclinical IL-12 and IL-18 data at AACR
**2024**: Candidate nominations for IL-12 and IL-18

### 2025

**1Q:** Interim OS for ARTISTRY-7 (Phase 3, PROC)[1]
**1H:** TLR Cohort 2 of ARTISTRY-6 (Phase 2, MM)[2]
**1H:** TLR Cohort 3-mono of ARTISTRY-6 (Phase 2, CM)[2]
**2H:** TLR Cohort 3-combo of ARTISTRY-6 (Phase 2, CM)[2]

1. Subject to patient enrollment and event accrual
2. Subject to patient enrollment



Abbrev.: **CM**: cutaneous melanoma; **IL-12:** interleukin-12; **IL-18:** interleukin-18; **MM**: mucosal melanoma; **OS**: overall survival; **PROC**: platinum resistant ovarian cancer; **RP2D**: recommended phase 2 dose; **TLR**: topline results



MURAL ONCOLOGY

# Industry Leading Management Team and Board of Directors

## Executive Team

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CEO

glympse bio · Bristol Myers Squibb · MERCK · PhRMA RESEARCH PROGRESS HOPE

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CFO

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EXELIXIS · Bristol Myers Squibb · MERCK · FDA

Maiken Keson-Brookes
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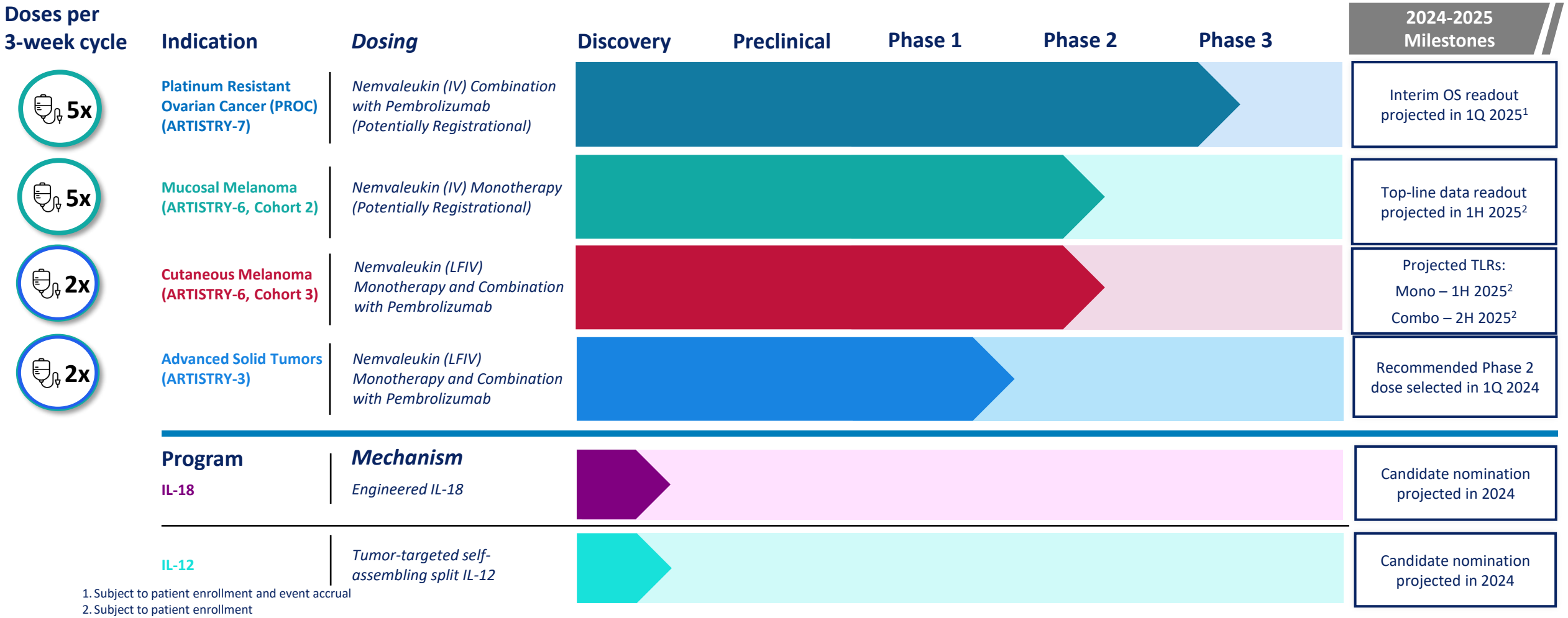
# Pipeline Overview: 2024-2025 Milestones




1. Subject to patient enrollment and event accrual
2. Subject to patient enrollment



Abbrev.: **IL**: interleukin; **IV**: intravenous; **LFIV:** less frequent IV dosing; **OS**: overall survival; **TLR**: topline readout



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# Mural's Novel Approach to Cytokine Design Seeks to Elevate Immunotherapy Treatment for Cancer Patients

**Immunotherapy (IO) has transformed oncology over the last few decades and continues to generate staggering sales**

>$100 B

Projected by 2027[1]

**Despite the progress of IO treatment, most patients fail to benefit from current treatments**

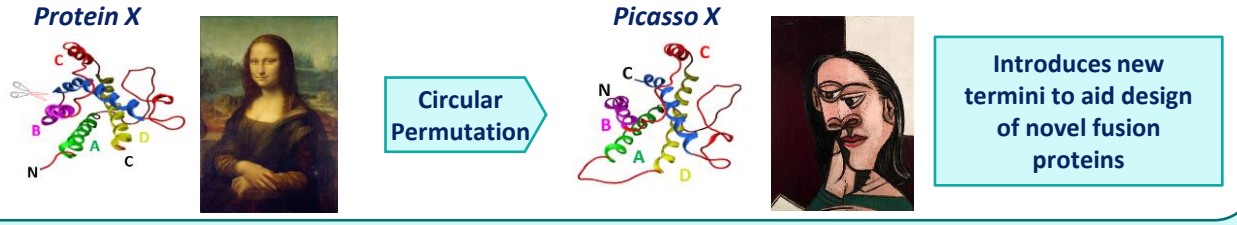
- Minority of patients respond to anti-PD-(L)1 therapy
- Responders often experience disease progression

**Developing elegantly engineered cytokines to unlock the promise of IO for broader cancer populations**

**Deep Biologic Understanding** → **Sophisticated Fit-for-purpose Protein Engineering** → **Elegantly Designed Cytokines**

*Developed to meaningfully enhance utility of selected protein*

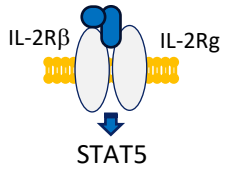
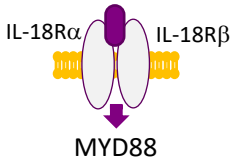
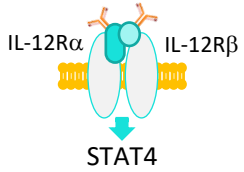
**Foundational Approach:** Proprietary "Picasso" Technology




Extracted from Lei Q, et al. Front. Cell Dev. Biol. 2020;8:00672

1. GlobalData Thematic Research: Immuno-Oncology

# Mural's Core Competency: Fit-For-Purpose Engineered Cytokines

| Program | | Technical challenge | Protein engineering solution |
|---|---|---|---|
| Nemvaleukin (IL-2 fusion protein) |  | • Systemic toxicities due to preferential binding to immunosuppressive high-affinity IL-2R | • Fusion of circularly permuted IL-2 with IL-2Rα subunit resulting in only activating immunostimulatory intermediate-affinity IL-2R |
| Engineered IL-18 |  | • Limited clinical efficacy due to IL-18BP tightly binding to IL-18, neutralizing IL-18 receptor activation | • Engineered IL-18 designed with a half-life extension and resistant to IL-18BP neutralization, while retaining native IL-18 activity |
| Tumor-targeted split IL-12 |  | • Clinical utility limited by severe toxicities at efficacious doses | • Separate inactive tumor-targeted IL-12 subunits that preferentially assemble and activate in the tumor |



Abbrev.: $T_{regs}$: regulatory T cells; **rhIL:** recombinant human IL; **IL-2R:** IL-2 receptor; **IL-2Rα**: IL-2R alpha, **IL-18BP:** IL-18 binding protein



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SECTION 2:

# NEMVALEUKIN ALFA

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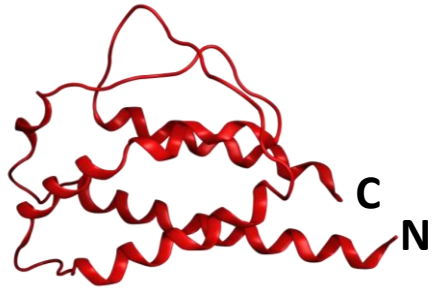
# IL-2: Known Clinical Potential and Drawbacks

**IL-2 with locations of N and C termini**




## Clinical Promise

- ✓ Monotherapy responses in cancer
  *Unusually durable responses in some patients*
- ✓ T and NK cell expansion and activation
- ✓ Potential to be used in CPI naïve and refractory settings

## Limitations Preventing Broader Clinical Use

- Toxic adverse event profile
  *Including cases of capillary leak syndrome*
- Short half-life
  *Requires frequent dosing & in-patient administration*
- Elevated $T_{regs}$ levels
  *Can lead to immune suppression*



Abbrev.: **CPI**: checkpoint inhibitor; **IL-2:** interleukin 2; **NK**: natural killer; **Tregs**: regulatory T cells



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# Nemvaleukin Design Detail

Thoughtful Selection of α Subunit for Fusion to IL-2

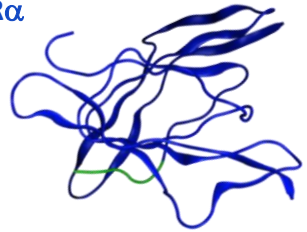
Application of Proprietary PICASSO™ Technology

Circular Permutation

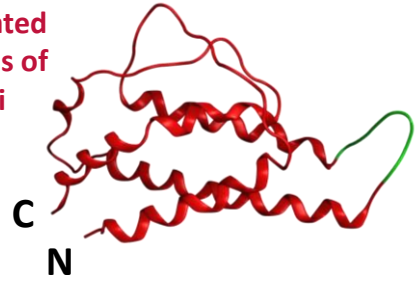
**Nemvaleukin**

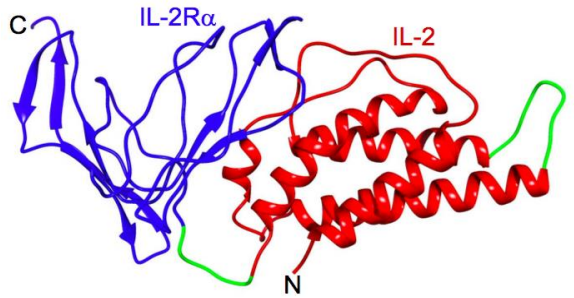
*Elegantly-designed fusion protein harnessing IL-2 immunostimulant biology*

**IL-2Rα**



**Circularly permutated IL-2 - new locations of N and C termini**




- Directly blocks α component of high affinity IL-2R
- Native component of IL-2 receptor complex

- **Minimal alteration to IL-2 sequence**
  - Allows appropriate placement of α subunit
- **Maintains IL-2 structure**
  - Preserves confirmation and activity at intermediate affinity IL-2R



Abbrev.: **IL-2R**: IL-2 receptor; **IL-2Rα:** IL-2R alpha



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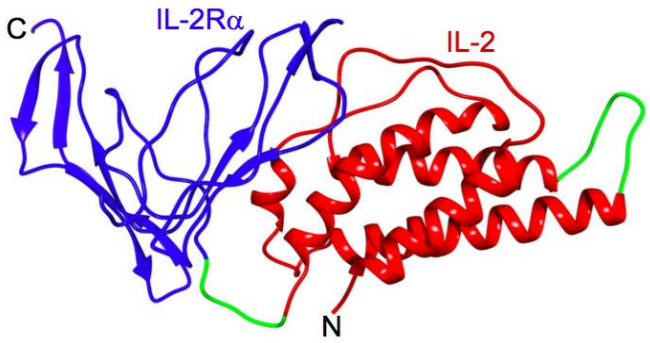
# Nemvaleukin's Design Differentiates It from Other IL-2 Approaches with the Potential to be First-in-Class

## Nemvaleukin




## Key Differentiators vs IL-2 Variant Approaches

- ✓ Durable, confirmed responses across broad range of tumors
  *Monotherapy and in combination (in CPI experienced population)*
- ✓ Immediately active
  *No metabolic conversion required*
- ✓ In two potentially registrational trials
  *Platinum resistant ovarian cancer and mucosal melanoma*

**Other IL-2 Variant Approaches:**

- Shielding
- Prodrug
- Masking
- Pegylation

X Require activation upon dosing
X Degrade to IL-2
X Include non-native components



Abbrev: **CPI**: checkpoint inhibitor; **IL-2:** interleukin-2



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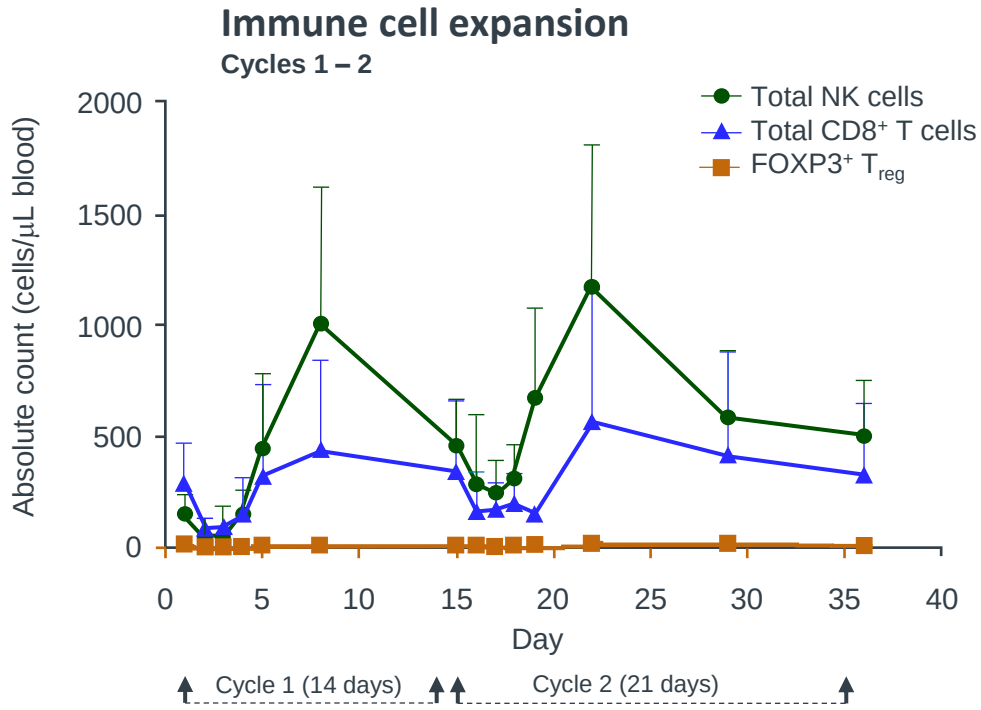
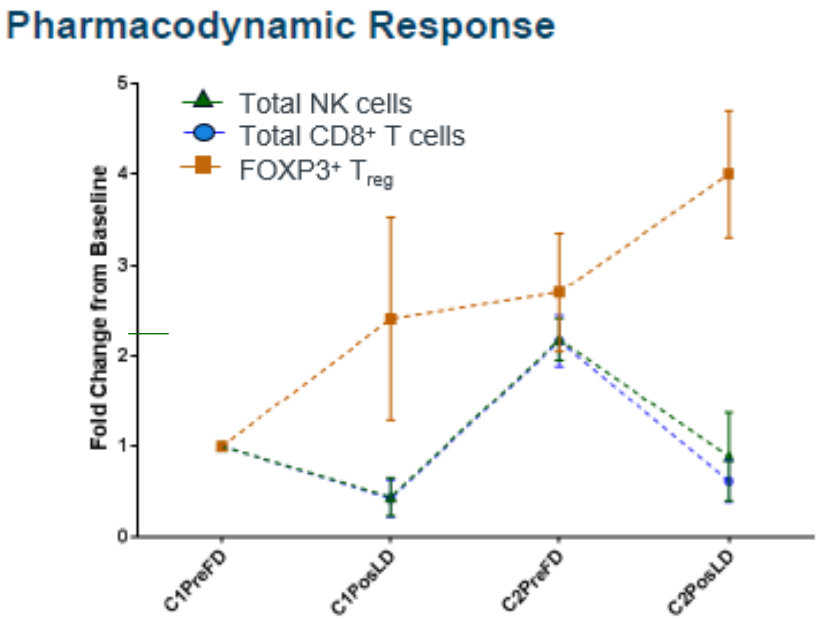
# Clinical Pharmacodynamic Effects of Nemvaleukin: More NK Cells and Fewer $T_{regs}$ than High-Dose IL-2[1,2]

## Nemvaleukin[1]




## High-Dose IL-2[2]




High-dose IL-2 33 µg/kg IV TIDx5

**Nemvaleukin: CD8 T and NK cells preferentially activated while $T_{regs}$ remained suppressed**

Nemvaleukin data are from the 6 µg/kg cohort in Part A of ARTISTRY-1. For fold change plots, data are mean + SE (N=10). For time course plot, data are mean + SD (N=12).

1. Vaishampayan et al. Oral Abstract 2500 presented at ASCO 2022. 2. Bhatt et al. Poster P123 presented at SITC 2018. Abbrev: **HD**: high-dose; **IL-2**: interleukin-2; **IV**: intravenous; **NK**: natural killer; **SD**: Standard deviation; **SE**: Standard Error; **TID**: 3 times daily; **Tregs**: regulatory T cells





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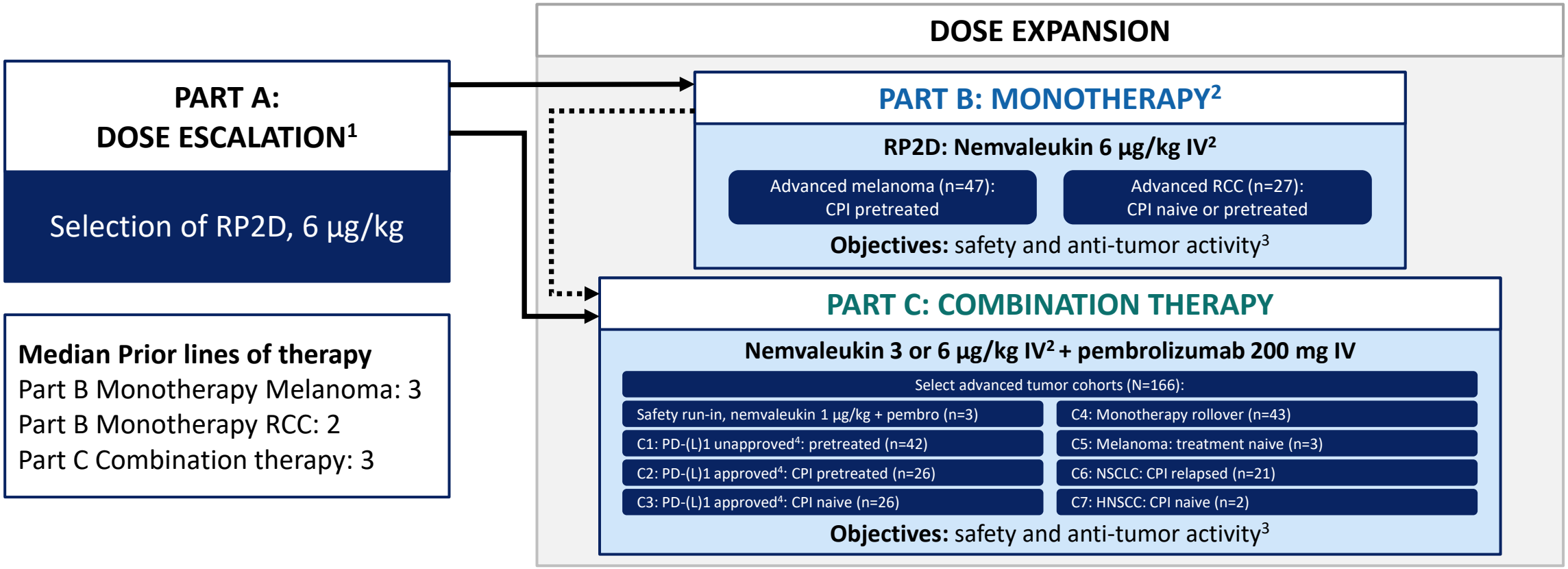
# ARTISTRY-1: First-In-Human Trial of IV Nemvaleukin
# Global, Multicenter, Open-Label Phase 1/2 Trial




NCTO2799095

1. Patients from Parts A and B could roll over to Part C upon progression or stable disease (after ≥ 4 cycles) on monotherapy
2. Nemvaleukin daily Q5D, then off treatment for 9 days (cycle 1) or 16 days (cycle 2+)
3. ORR assessed by investigator (RECIST v1.1)
4. Nemvaleukin 3 µg/kg/d in C1-C4, 6 µg/kg/d in C5-C7. PD-(L)1 approved/unapproved indication based on FDA prescribing information and may have changed over time



**Abbrev.: C1-7**: Cohorts 1-7; **CPI**: checkpoint inhibitor; **HNSCC**: head & neck squamous cell carcinoma; **IV**: intravenous; **NSCLC**: non-small cell lung cancer; **ORR**: overall response rate; **PD-(L)1**: programmed death (ligand) 1; **RCC**: renal cell carcinoma; **RECIST**: Response Evaluation Criteria In Solid Tumors; **RP2D**: recommended phase 2 dose



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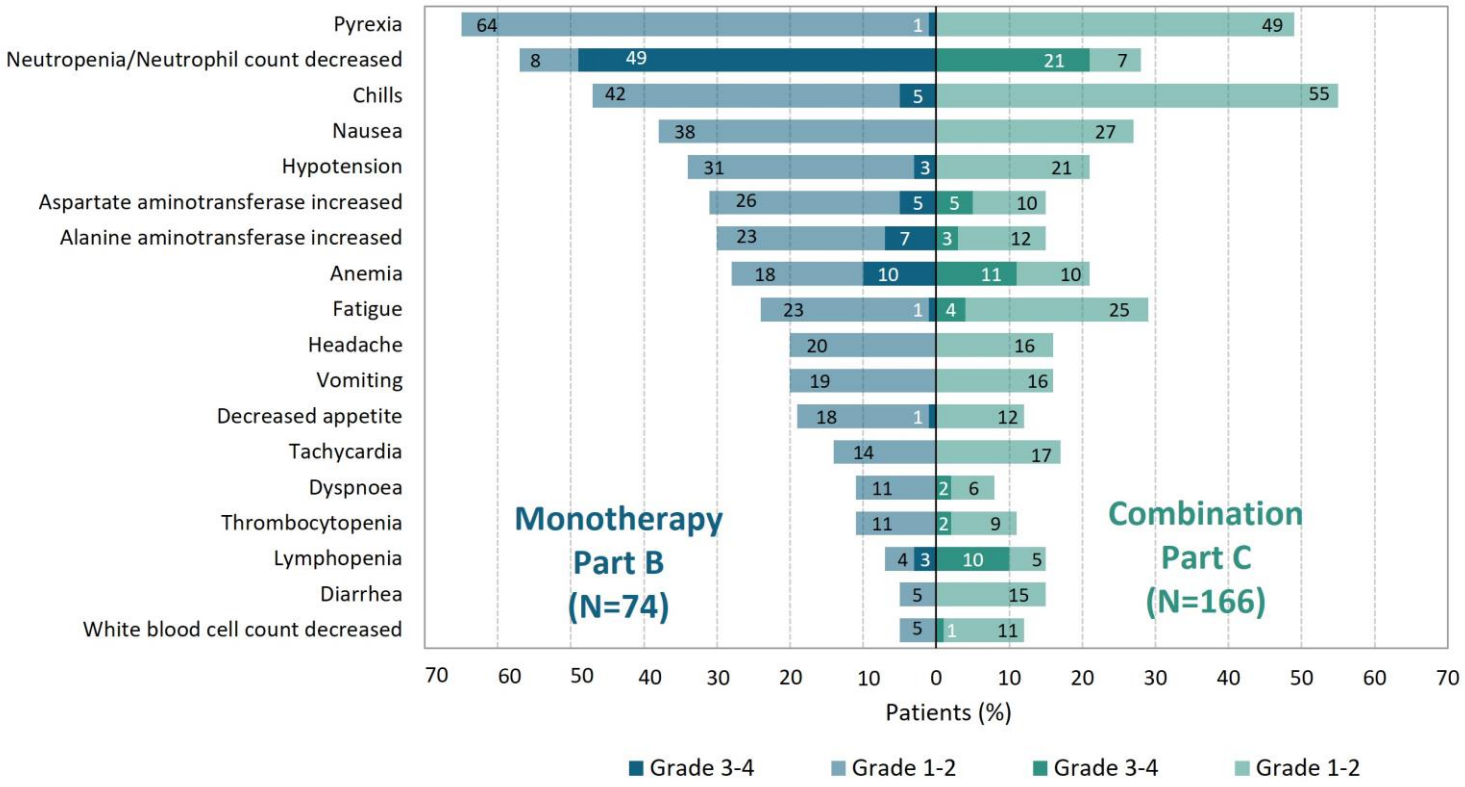
# Nemvaleukin's Adverse Event Profile in ARTISTRY-1 Was Consistent with Our Expectations Based on its Mechanism of Action




- Administered on outpatient basis; most frequent AEs were manageable with supportive care
- AE profile consistent with nemvaleukin mechanism of action
- Monotherapy safety profile was similar to combination, with no additive toxicity
- Most frequently observed grade 3-4 TRAE: neutropenia[1]
  - Median duration 4 days; not associated with risk of serious infections or febrile neutropenia
- TRAEs leading to discontinuation: 4% (monotherapy)[2], 4% (combination)[3]

1. Includes neutropenia and neutrophil count decreased
2. TRAEs leading to discontinuation in monotherapy were Gr3 failure to thrive, Gr3 bronchospasm, Gr2 ECG T wave abnormal, and Gr1 cardiac troponin increase
3. TRAEs leading to discontinuation in combination were Gr5 starvation, Gr3 arthralgia, Gr3 fatigue, Gr3 pneumonia, and Gr2 cytokine release syndrome

Part C includes patients who received nemvaleukin at 1, 3, or 6 µg/kg IV in combination with pembrolizumab 200 mg IV. Data as of Mar 27, 2023


Data as of March 27, 2023

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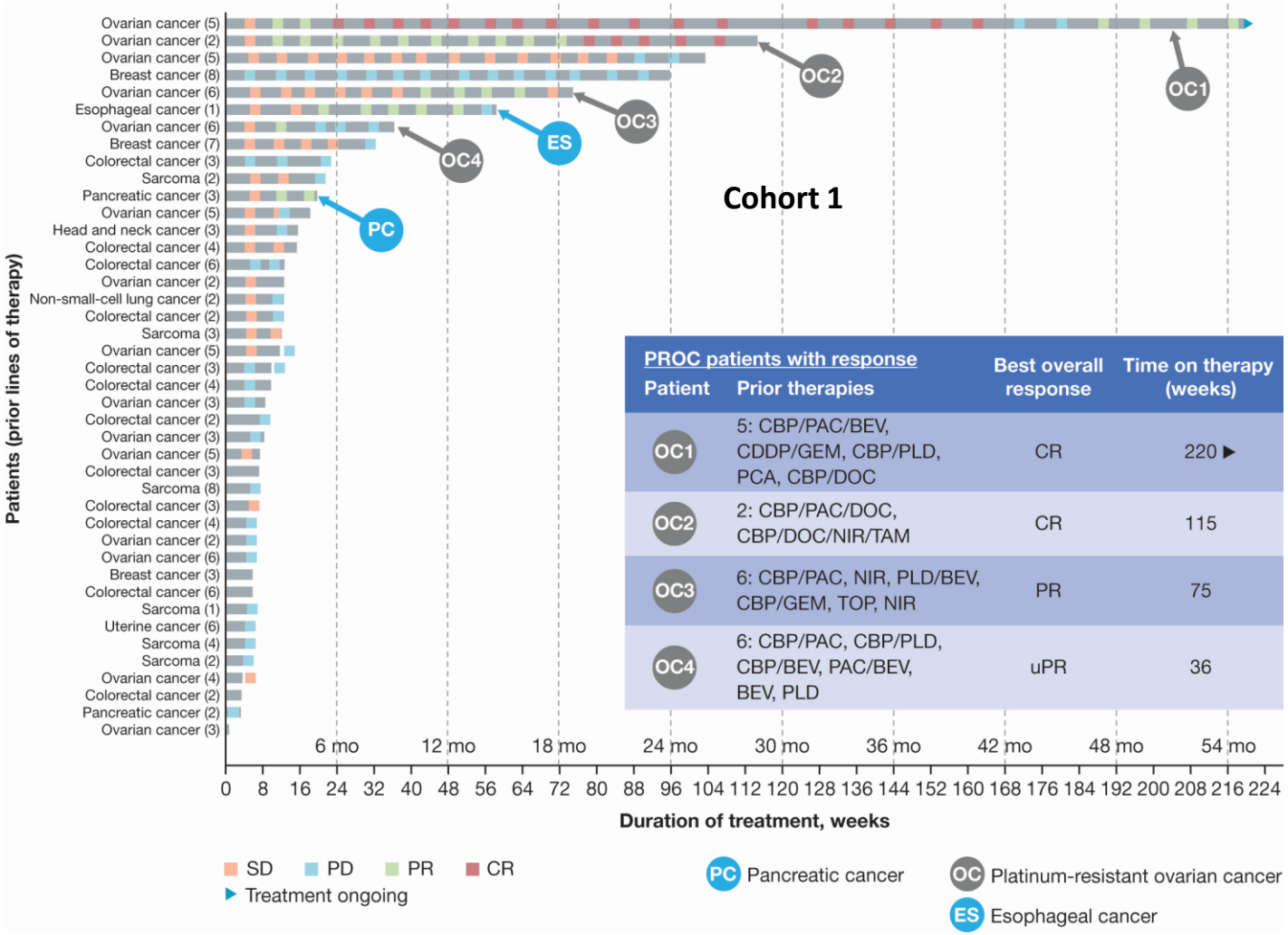
# ARTISTRY-1: Nemvaleukin Combination Treatment with Pembrolizumab Demonstrated Durable Responses




| Best overall response n (%) | PROC (n=14) |
|---|---|
| CR | 2 (14.3%) |
| PR | 2 (14.3)* |
| SD | 6 (42.9) |
| PD | 2 (33.3) |
| ORR, n (%) | 4 (28.6)* |
| DCR, n (%) | 10 (71.4)* |
| Median DOR in weeks | 65.5 |

* Includes 1 confirmed PR, 1 unconfirmed PR

Of the 14 evaluable, investigator reported PROC patients, the median prior lines of ovarian cancer therapy was 5

Data cut off Mar 27 2023

Abbrev.: **BEV**: bevacizumab; **CBP**: carboplatin; **CDDP**: cisplatin; **CR:** complete response; **DOC**: docetaxel; **FDA**: Food and Drug Administration; **GEM**: gemcitabine; **mo**: month; **NIR**: niraparib; **PAC**: paclitaxel; **PCA**: paclitaxel albumin; **PD**: progressive disease; **PD-(L)1**: programmed death (ligand) 1; **PLD**: pegylated liposomal doxorubicin hydrochloride; **PR**: partial response; **PROC**: platinum-resistant ovarian cancer; **SD**: stable disease; **TAM**: tamoxifen; **TOP**: topotecan; **uPR**: unconfirmed PR





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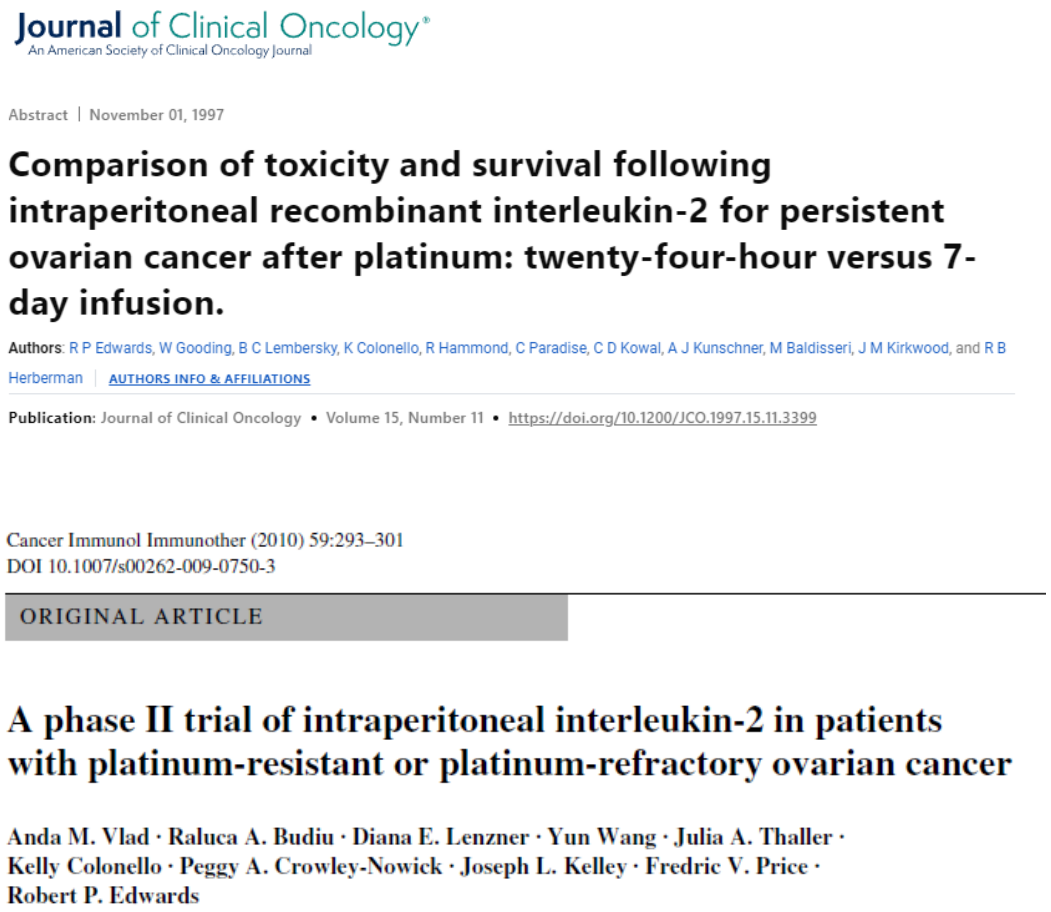
# Rationale Underpinning Use of Nemvaleukin in PROC



Journal of Clinical Oncology
An American Society of Clinical Oncology Journal

Abstract | November 01, 1997

**Comparison of toxicity and survival following intraperitoneal recombinant interleukin-2 for persistent ovarian cancer after platinum: twenty-four-hour versus 7-day infusion.**

Authors: R P Edwards, W Gooding, B C Lembersky, K Colonello, R Hammond, C Paradise, C D Kowal, A J Kunschner, M Baldisseri, J M Kirkwood, and R B Herberman | AUTHORS INFO & AFFILIATIONS

Publication: Journal of Clinical Oncology • Volume 15, Number 11 • https://doi.org/10.1200/JCO.1997.15.11.3399

Cancer Immunol Immunother (2010) 59:293–301
DOI 10.1007/s00262-009-0750-3

ORIGINAL ARTICLE

**A phase II trial of intraperitoneal interleukin-2 in patients with platinum-resistant or platinum-refractory ovarian cancer**

Anda M. Vlad · Raluca A. Budiu · Diana E. Lenzner · Yun Wang · Julia A. Thaller · Kelly Colonello · Peggy A. Crowley-Nowick · Joseph L. Kelley · Fredric V. Price · Robert P. Edwards

In two peer-reviewed, intraperitoneal trials of recombinant IL-2 in ovarian cancer:

- 1997 JCO paper
  - 26% ORR (6 CRs, 3 PRs in 35 evaluable patients)
  - Median survival time of responders was not reached at time of publication (range, 27 to 90+ mos)

- 2010 CII paper
  - 25% ORR (4 CRs, 2 PRs in 24 evaluable patients)
  - OS of 2.1 years with one responder surviving for 10 years



Abbrev.: **CII**: *Cancer Immunology, Immunotherapy*; **CR**: complete response; **IL-2**: interleukin-2; **JCO**: *Journal of Clinical Oncology*; **ORR**: overall response rate; **OS**: overall survival; **PR**: partial response; **PROC**: platinum resistant ovarian cancer



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# ARTISTRY-7: Phase 3 / Potentially Registrational Study for Platinum-Resistant Ovarian Cancer

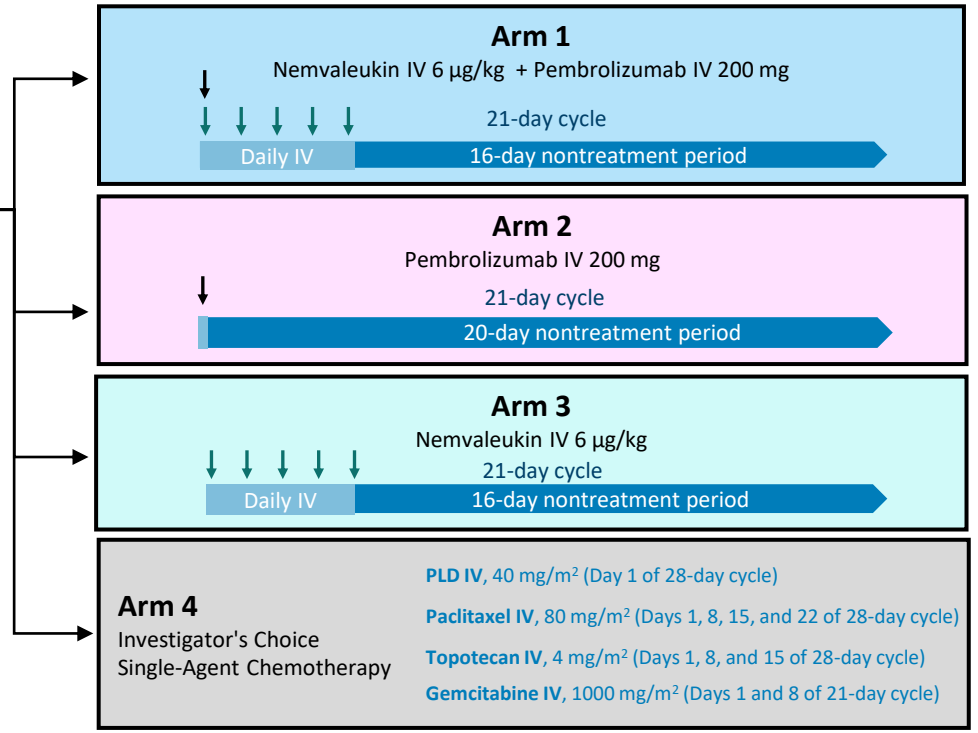
## Investigational Nemvaleukin IV + Pembrolizumab versus Chemotherapy

Estimated 448 participants

Randomization
3:1:1:3
Futility analysis planned for monotherapy arms [1]

### Key eligibility criteria

- Platinum-resistant/refractory epithelial ovarian, fallopian tube, or primary peritoneal cancer
- At least 1L of systemic platinum therapy and ≤5L of systemic platinum-resistant therapy
- Prior bevacizumab treatment
- Measurable disease by RECIST v1.1




### Key Endpoints

**Primary outcome measure:**

- Overall survival (OS)

**Secondary outcome measures:**

- PFS, ORR, DCR, DOR, and TTR
- CA-125 response
- TEAEs

Clinical trial and supply agreement with MSD (a tradename of Merck & Co., Inc. Rahway, NJ, USA)

Conduct of trial is in association with The GOG Foundation, Inc. (GOG), the European Network of Gynaecological Oncological Trial groups (ENGOT), and the Asia-Pacific Gynecologic Oncology Trials Group (APGOT)

↓ Pembrolizumab dosing ↓ Nemvaleukin dosing

[a] Alternative topotecan regimen: 1.25 mg/m² on Days 1-5 of 21-d cycles
[b] Response per RECIST v1.1
[c] Response per GCIG

1. Herzog T et al. Poster presented at the Society for Gynecologic Cancers Annual Meeting (SGO), Phoenix, AZ, March 18-21, 2022

Abbrev.: **CA-125**: cancer antigen-125; **DCR**: disease control rate; **DOR**: duration of response; **GCIG**: Gynecologic Cancer InterGroup; **IV**: intravenous; **ORR**: objective response rate; **PFS**: progression-free survival; **PLD**: pegylated liposomal doxorubicin; **RECIST**: Response Evaluation Criteria in Solid Tumors; **TEAE**: treatment-emergent adverse event; **TTR**: time to response





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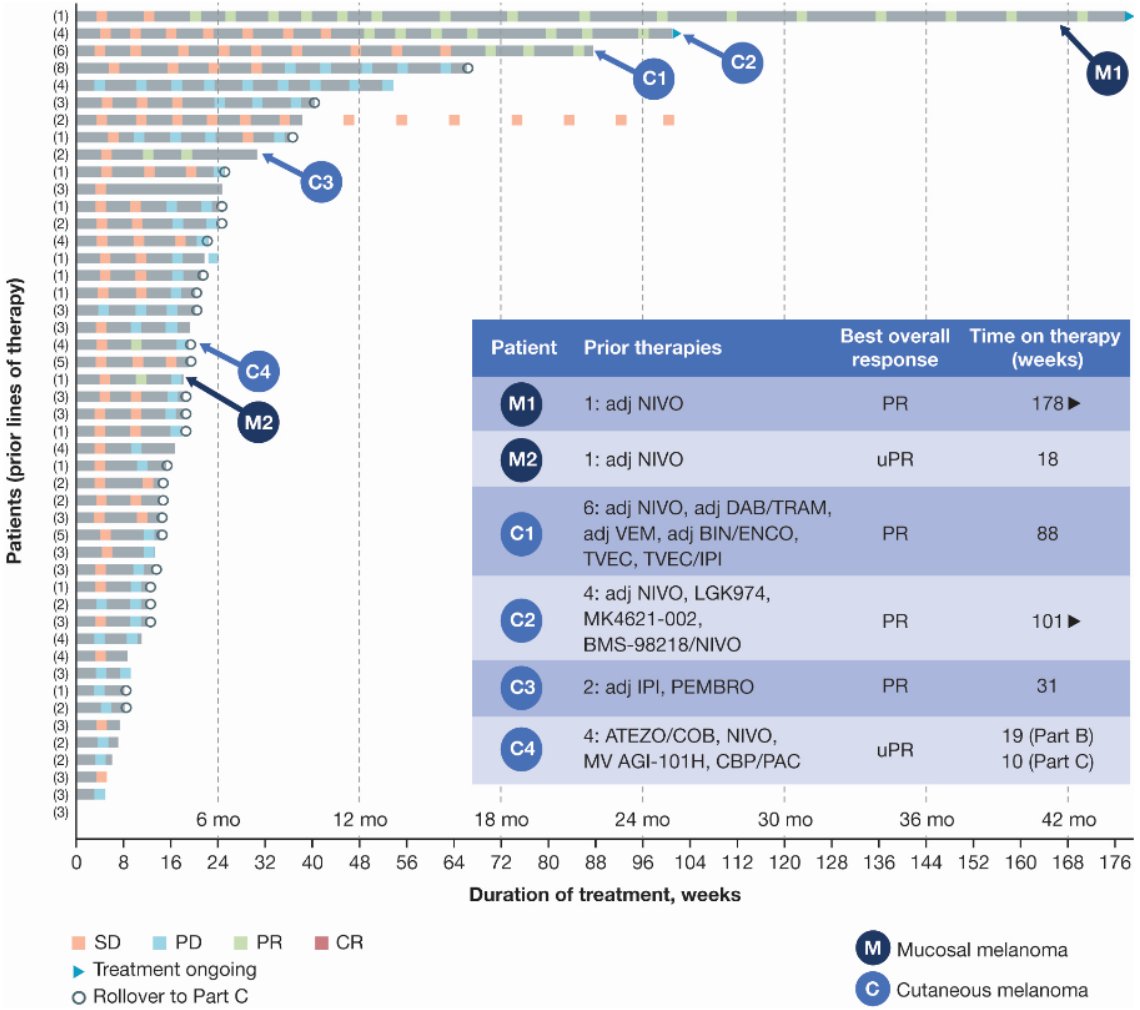
# ARTISTRY-1: Nemvaleukin Demonstrated Durable Monotherapy Responses in Melanoma (Part B)




| | All[a,b] (n=46) | Mucosal (n=6) |
|---|---|---|
| Best overall response, n (%) | | |
| CR | 0 | 0 |
| PR | 6 (13.0)[c] | 2 (33.3)[d] |
| SD | 30 (65.2) | 2 (33.3) |
| PD | 10 (21.7) | 2 (33.3) |
| ORR, n (%) [95% CI] | 6 (13.0) [4.9-26.3][c] | 2 (33.3) [4.3-77.8][d] |
| DCR, n (%) [95% CI] | 36 (78.3) [63.6-89.1] [c] | 4 (66.7) [22.3-95.7] [d] |
| DOR in weeks[d], Mean (SD)<br>Median (range) | 40.77 (55.6) [c]<br>16.75 (6.1-150.3) | 78.2 (101.9)[d]<br>78.2 (6.1-150.3) |

[a] Excludes 1 patient who did not meet tumor-evaluable criteria. [b] Patients with mucosal, cutaneous, uveal, acral included in 'All'. [C] Includes 4 confirmed PRs, 2 unconfirmed PRs, [d] 1 confirmed PR. [e] DOR for Part B only and does not include patients who rolled over to Part C; some patients may still be on treatment

- All responders had been on prior CPI therapy and progressed
- FDA Orphan Drug and Fast Track designations, as well as MHRA's ILAP Innovation Passport, granted in mucosal melanoma
- Data supported design of ARTISTRY-6 study

Data cut off Mar 27, 2023

Abbrev.: **adj**: adjuvant; **ATEZO**: atezolizumab; **BIN**: binimetinib; **CBP**: carboplatin; **CI**: confidence interval; **COB**: cobimetinib; **CPI**: checkpoint inhibitor; **CR**: complete response; **DAB**: dabrafenib; **DCR**: disease control rate (CR+PR+SD); **DOR**: duration of response; **ENCO**: encorafenib; **FDA**: US Food and Drug Administration; **IPI**: ipilimumab; **MHRA:** Medicines and Healthcare products Regulatory Agency; **MV**: melanoma vaccine; **NA**: not applicable; **NIVO**: nivolumab; **ORR**: overall response rate; **PAC**: paclitaxel; **PD**: progressive disease; **PEMBRO**: pembrolizumab; **PR**: partial response; **SD**: stable disease; **TRAM**: trametinib; **TVEC**: talimogene laherparepvec; **VEM**: vemurafenib





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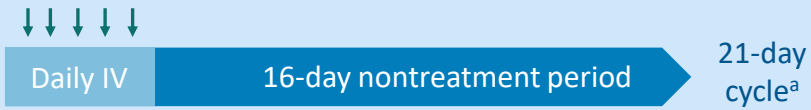
# Cohort 2 of ARTISTRY-6: Phase 2 / Potentially Registrational Trial of Nemvaleukin in Mucosal Melanoma

### Key eligibility criteria [1]

- Unresectable and/or metastatic mucosal melanoma
- Patient has received anti–PD(L)-1 ± anti–CTLA-4 therapy
- No more than 1 prior systemic therapy
- Measurable disease per RECIST v1.1
- ECOG PS 0-1

**Cohort 2**
Mucosal melanoma (N=90)
Nemvaleukin IV 6 µg/kg QDx5 Monotherapy




### Key endpoints

- **Primary:** ORR per RECIST v1.1 (by independent central review)
- **Key secondary:** DOR, PFS, DCR, TTR per RECIST v1.1 (by independent central review)

[a] With the exception of Cycle 1, which is 14 days (daily IV for 5 days + 9 days nontreatment), all cycles were 21 days[3]

↓ Nemvaleukin dosing

- ARTISTRY-6 also includes Cohorts 1 and 3 which are designed to explore alternative dosing regimens of nemvaleukin in cutaneous melanoma

1. https://clinicaltrials.gov, NCT04830124



Abbrev.: **CTLA-4:** cytotoxic T-lymphocyte–associated antigen 4; **DCR**: disease control rate; **DOR**: duration of response; **ECOG PS**: Eastern Cooperative Oncology Group performance status; **IV**: intravenous; **ORR**: objective response rate; **PD-(L)1**: programmed death (ligand) 1; **PFS**: progression-free survival; **RECIST**: Response Evaluation Criteria in Solid Tumors; **TTR**: time to response



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# Exploration of Alternative Dose Administration and Schedule Underway to Further Optimize Nemvaleukin Profile


**5X daily (Days 1-5) Q3W**
Dosing modeled after approved high-dose IL-2

**ARTISTRY-1**
Phase 1/2
Monotherapy / Dose Escalation / Expansion / Combination

**Cohort 2 of ARTISTRY-6**
Phase 2
Mucosal Melanoma

**ARTISTRY-7**
Phase 3
PROC


**2X daily (Days 1 and 8) Q3W**
Improved patient-friendly dosing schedule

**ARTISTRY-3**
Phase 1 Monotherapy - explored 1X and 2X Q3W
**RP2D selected 1Q 2024**

**Cohort 3 of ARTISTRY-6**
Phase 2
Cutaneous Melanoma

**Future Nemvaleukin Clinical Trials**


Abbrev.: **PROC**: platinum-resistant ovarian cancer; **RP2D**: recommended phase 2 dose



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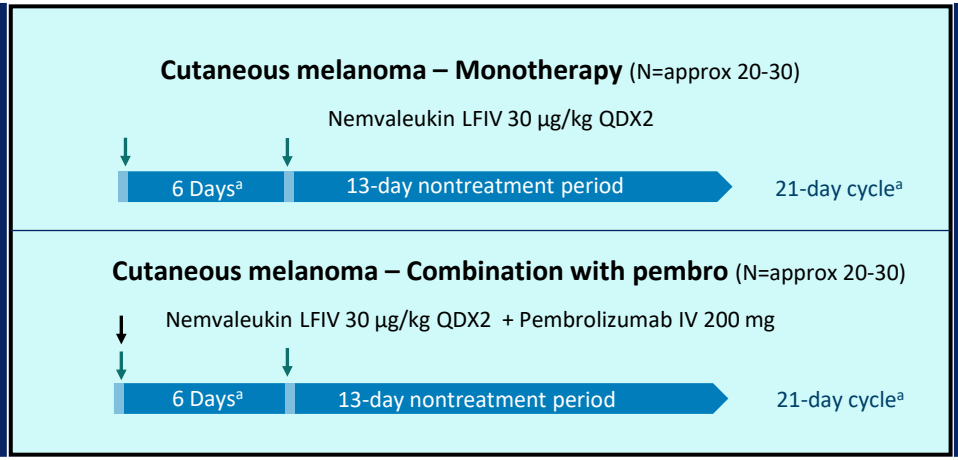
# Cohort 3 of ARTISTRY-6: Phase 2 Trial in Cutaneous Melanoma

**Investigational Nemvaleukin LFIV Monotherapy ± Pembrolizumab[1]**

## Key eligibility criteria[1]

- Unresectable and/or metastatic cutaneous melanoma
- Patient has received anti–PD(L)-1 ± anti–CTLA-4 therapy
- No more than 1 prior systemic therapy
- Measurable disease per RECIST v1.1
- ECOG PS 0-1




## Key endpoints (independent of cohort)[2]

- **Primary:** ORR per RECIST v1.1 (by independent central review)
- **Key secondary:** DOR, PFS, DCR, TTR per RECIST v1.1 (by independent central review)

Pembrolizumab dosing  Nemvaleukin dosing

a. Nemvaleukin dosing twice Q3W to be days 1 and 8 Q3W

- ARTISTRY-6 also includes Cohort 1 which is designed to explore subcutaneous dosing regimen of nemvaleukin in cutaneous melanoma

1. https://clinicaltrials.gov, NCT04830124
2. Lewis K, et al. Presentation at the Melanoma and Immunotherapy Bridge 2021 Virtual Congress; December 1-4, 2021

Abbrev.: **CTLA-4:** cytotoxic T-lymphocyte–associated antigen 4; D1/4: days 1 and 4; **DCR**: disease control rate; **DOR**: duration of response; **ECOG PS**: Eastern Cooperative Oncology Group performance status; **IV**: intravenous; **LFIV**: less frequent IV; **ORR**: objective response rate; **PD-(L)1**: programmed death (ligand) 1; **PFS**: progression-free survival; **Q3W**: 3-week cycle; **QDX2**: two doses, one each day ; **RECIST**: Response Evaluation Criteria in Solid Tumors; **TTR**: time to response.





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# Focused on Initial, Potentially Registrational Indications with Compelling Expansion Opportunities

## Initial Development

Two indications with unmet need

### Platinum-Resistant Ovarian Cancer

13K Patients[1,2]

- FDA Fast Track Designation
- In combination with pembrolizumab
- Potential to provide an immunotherapy option to an indication where CPIs have failed

### Mucosal Melanoma

2K Patients[1]

- FDA Fast Track and Orphan Drug Designation
- Opportunity to further establish monotherapy efficacy in a larger patient cohort
- Potential to be first approval specific to mucosal melanoma

## Planned Expansion Into Broader Cancer Indications

Evolution of a proven cytokine provides opportunity to expand utility

### Earlier Lines of Therapy in Ovarian and Cutaneous Melanoma

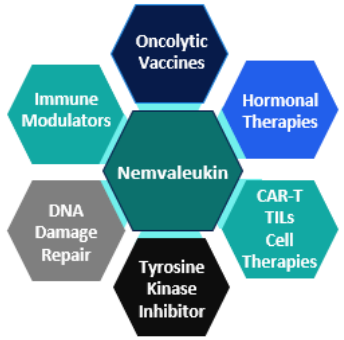
**40K+**

First line patients in each indication[1]

**Multiple complete and partial responses**

Observed in both cutaneous melanoma and ovarian cancer in combination with an anti-PD-(L)1 therapy

### Other Mechanistic Combinations




Scientific rationale for many combinations to advance cancer treatment across a range of tumor types

**Apply design and development approach to advance additional immunotherapy applications**

1. Clarivate Epidemiology; Estimated number of patients in the U.S. and Europe
2. Represents 3rd line PROC patients



Abbrev.: **CAR-T**: chimeric antigen receptor T-cell; **CPI**: checkpoint inhibitor; **PD-(L)1**: programmed death (ligand) 1; **TIL**: tumor-infiltrating lymphocyte



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SECTION 3:

# ADDITIONAL PIPELINE PROGRAMS

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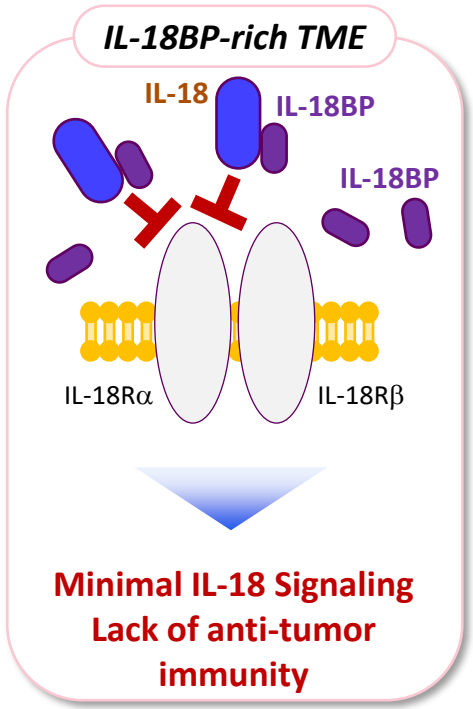
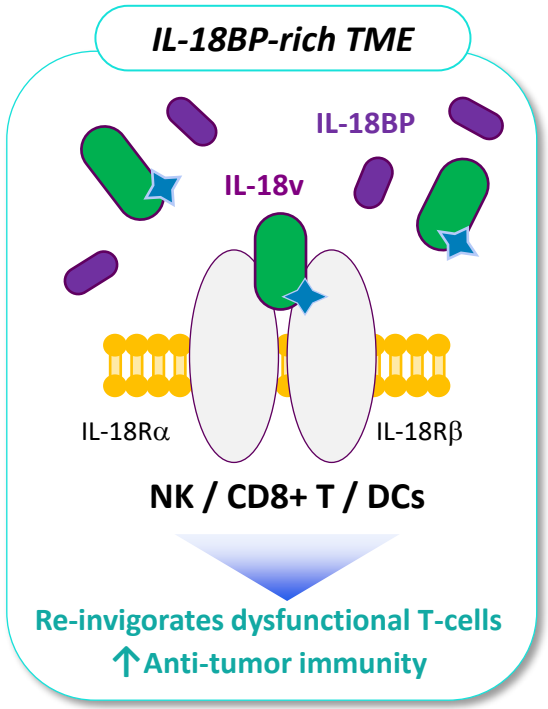
# IL-18 Engineering: Resist IL-18BP Checkpoint to Unleash the Therapeutic Potential of IL-18

## Challenge to IL-18




*Internal expertise in protein engineering*

## Mural Solution: Engineer IL-18 variants resistant to IL-18BP

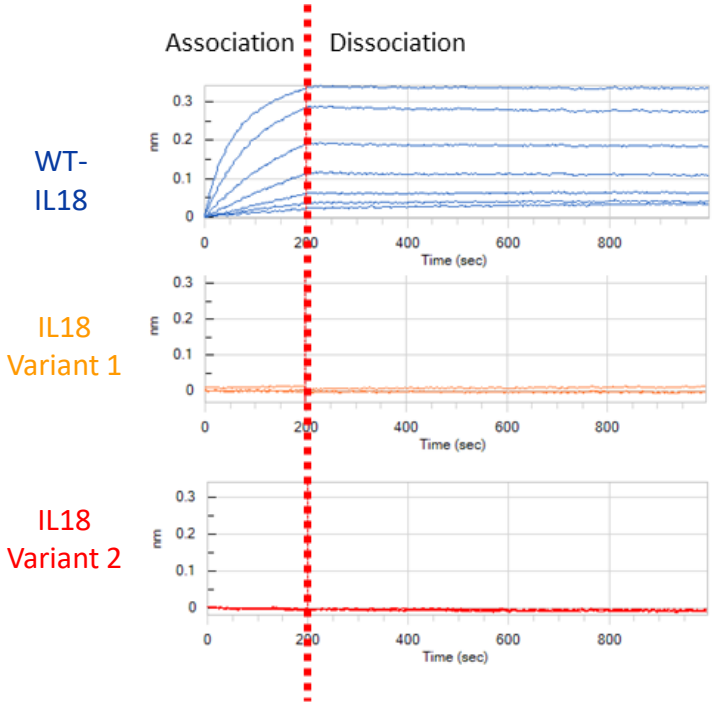



**Design Approach via Mutation(s):**

1. **Resist IL-18 neutralization by immune checkpoint IL-18BP**
2. **Retain and optimize IL-18 activity**
3. **Increase exposure via half-life extension**

# Preclinical Studies Demonstrated Improved Potency with Maximal Resistance to IL-18BP Inhibition

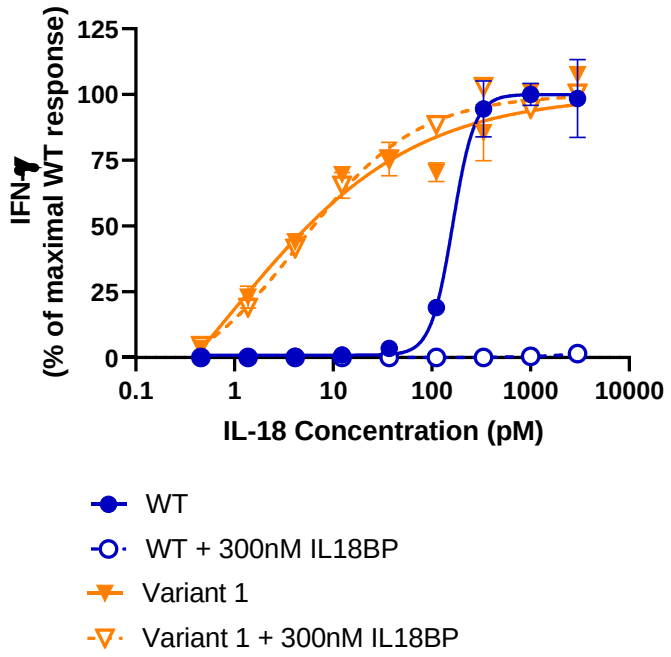
## No Detectable Binding of Variants to IL-18BP



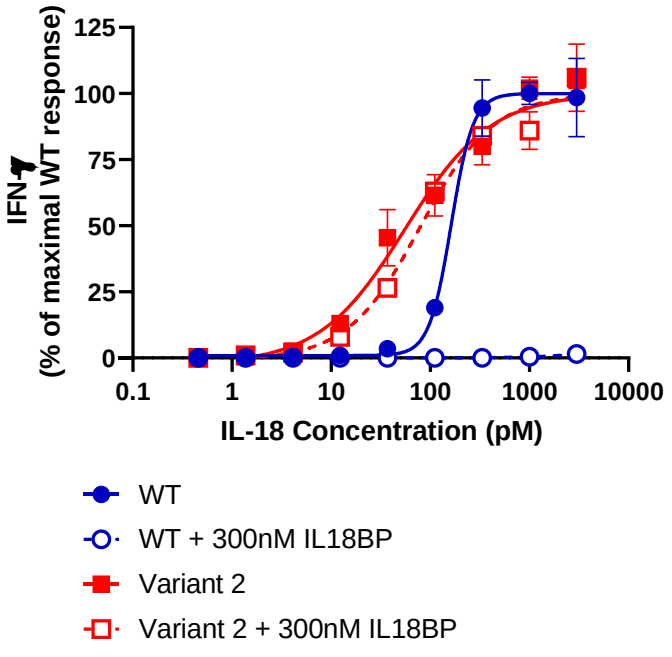

Note: No detectable binding of IL18 variants to hIL-18BP

## Variants with Broad Range of Potency vs WT IL-18 with Resistance to IL-18BP Suppression

**Maximal Resistance with Potency Stronger than WT**




**Maximal Resistance with Potency Similar to WT**




*Mural internal data

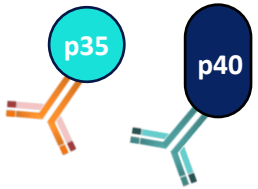
# IL-12 Engineering: Tumor Site-Specific Assembly of Functional IL-12 Designed to Limit Systemic IL-12 Exposure

**Assemble functional IL-12 in the tumor with goals of avoiding toxicity associated with systemic exposure and maximizing the IL-12 therapeutic window**

**IL-12 subunits are fused to Mural's antibody fragments**

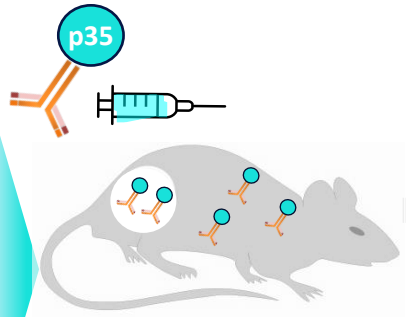
**Tumor-targeted IL-12 subunits**

Non-targeted engineered inactive subunits

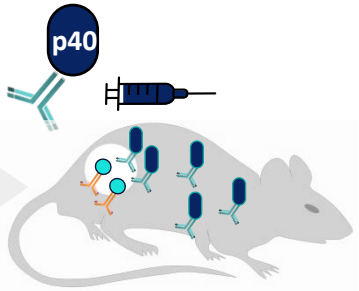



Tumor-targeting Antibody fragments

Treat with targeted **p35 subunit**




Treat with targeted **p40 subunit**

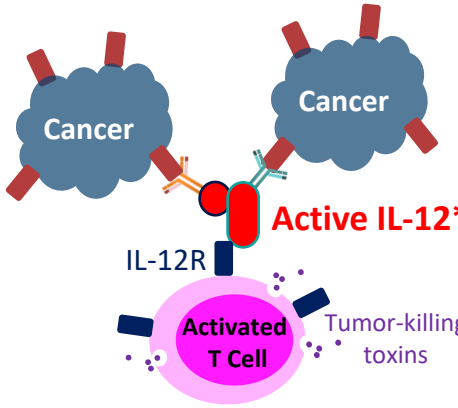



Clearance of systemic p35 subunits from circulation

Results in **active IL-12 in the tumor**

**Active IL-12 assembly *in situ***

Cancer cells expressing tumor antigen




*IL-12 subunits could be both cis- and trans-acting





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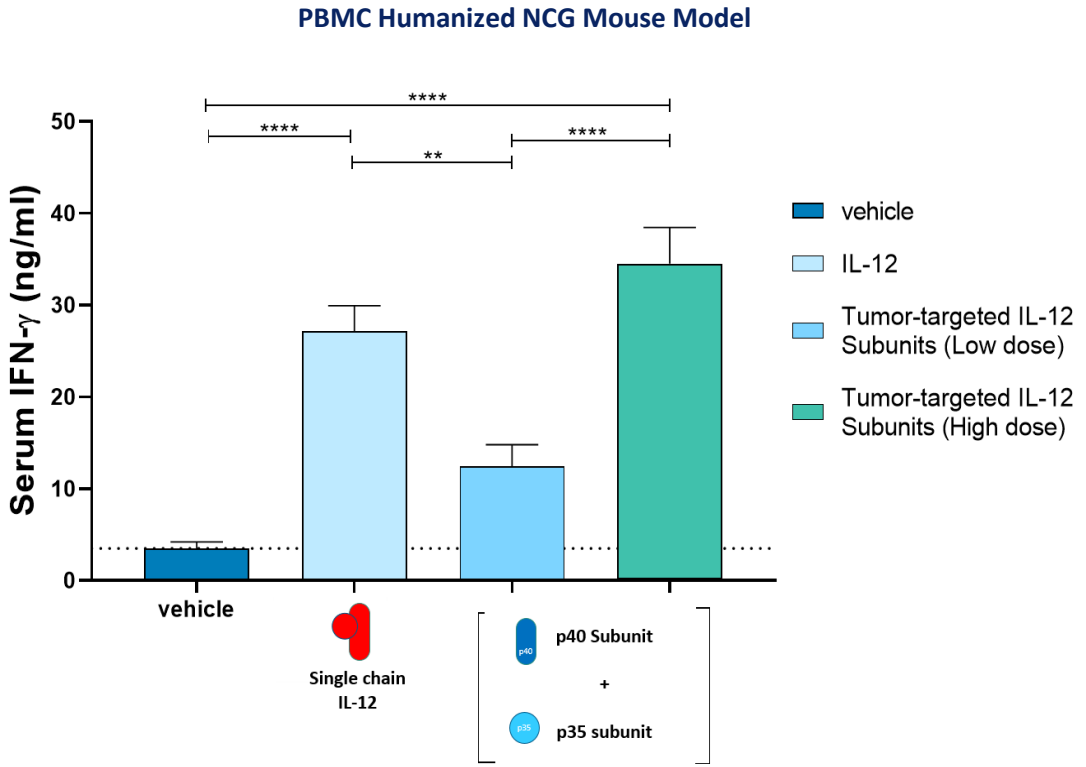
# Preclinical Studies Provide Proof of Mechanism with a Clear Pharmacodynamic Response

- In general, IL-12 anti-tumor activity observed in preclinical studies has been driven by activation of innate and adaptive immune compartments and production of IFN-γ[1,2]
  - Clinical utility has been limited by severe toxicities from systemic exposure leading to a narrow therapeutic index[1,2,3]
- Mural's sequential administration of tumor-targeted IL-12 subunits resulted in a dose-dependent increase in serum IFN-γ levels




1. Nguyen KG et. al. Cancer Immunotherapy. Front. Immunol. October 15 2020 11:575597
2. Vecchio MD et. al. Clin Cancer Res August 15 2007 (13) (16) 4677-4685
3. Strauss J et. al. Clin Cancer Res January 1 2019 (25) (1) 99-109

Source: Company internal data on file


Abbrev: **rhIL-12**: recombinant human IL-12; **GLP:** good laboratory practice



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# Mural Oncology

**Proprietary Cytokine Engineering Technology**
Proven to retain cytokine potency while overcoming limitations

Phase 2/3

**Late-Stage Clinical Biotech**
Lead asset (nemvaleukin) in two potentially registrational trials

**Well-Funded**
Cash runway into 4Q 2025

## Key Upcoming Catalysts

### 2024

✓ **1Q:** RP2D for next generation dosing schedule
**2Q:** Preclinical IL-12 and IL-18 data at AACR
**2024**: Candidate nominations for IL-12 and IL-18

### 2025

**1Q:** Interim OS for ARTISTRY-7 (Phase 3, PROC)[1]
**1H:** TLR Cohort 2 of ARTISTRY-6 (Phase 2, MM)[2]
**1H:** TLR Cohort 3-mono of ARTISTRY-6 (Phase 2, CM)[2]
**2H:** TLR Cohort 3-combo of ARTISTRY-6 (Phase 2, CM)[2]

1. Subject to patient enrollment and event accrual
2. Subject to patient enrollment



Abbrev.: **CM**: cutaneous melanoma; **IL-12:** interleukin-12; **IL-18:** interleukin-18; **MM**: mucosal melanoma; **OS**: overall survival; **PROC**: platinum resistant ovarian cancer; **RP2D**: recommended phase 2 dose; **TLR**: topline results



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# THANK YOU!

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