# INVESTOR PRESENTATION

November 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 IL-2, IL-12, and IL-18 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 IL-2, IL-12, and IL-18 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 Quarterly Report on Form 10-Q for the quarterly period ended September 30, 2024, and as may be updated 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: Building a New Class of Cytokine Therapies

Phase 2 & 3

**Late-Stage Trials:**
2 potentially registrational trials reading out 1H 2025

**Commercial Opportunity:**
2 indications with limited available therapies and planned indication expansion

**Pipeline Expansion:**
Advancing 2 preclinical programs, candidate nominations in 2024

**Cash Position:**
Runway into 4Q 2025

## Key Upcoming Catalysts

### 1H 2025

**Late Q1/Early Q2:** Interim OS for ARTISTRY-7[1] (potentially registrational)
**Q2:** TLR Cohort 2 of ARTISTRY-6 (potentially registrational)
**1H:** PDR Cohort 3-mono of ARTISTRY-6 (Phase 2, CM)[2]

### 2H 2025

**2H:** PDR Cohort 4-combo of ARTISTRY-6 (Phase 2, CM)[2]
**Q4:** IL-18 IND submission

1. Subject to 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; **PDR**: preliminary data readout; **PROC**: platinum resistant ovarian cancer; **RP2D**: recommended phase 2 dose; **TLR**: topline results



MURAL ONCOLOGY

# Highly Experienced Late-Stage Oncology Team

## Executive Team

**Caroline Loew, PhD**
**CEO**

**Adam Cutler**
**CFO**

**Vicki Goodman, MD**
**CMO**

**Maiken Keson-Brookes**
**CLO**

## Board of Directors

**Francis Cuss**
**MB, BChir, FRCP**

**Benjamin Hickey**
**MBA**

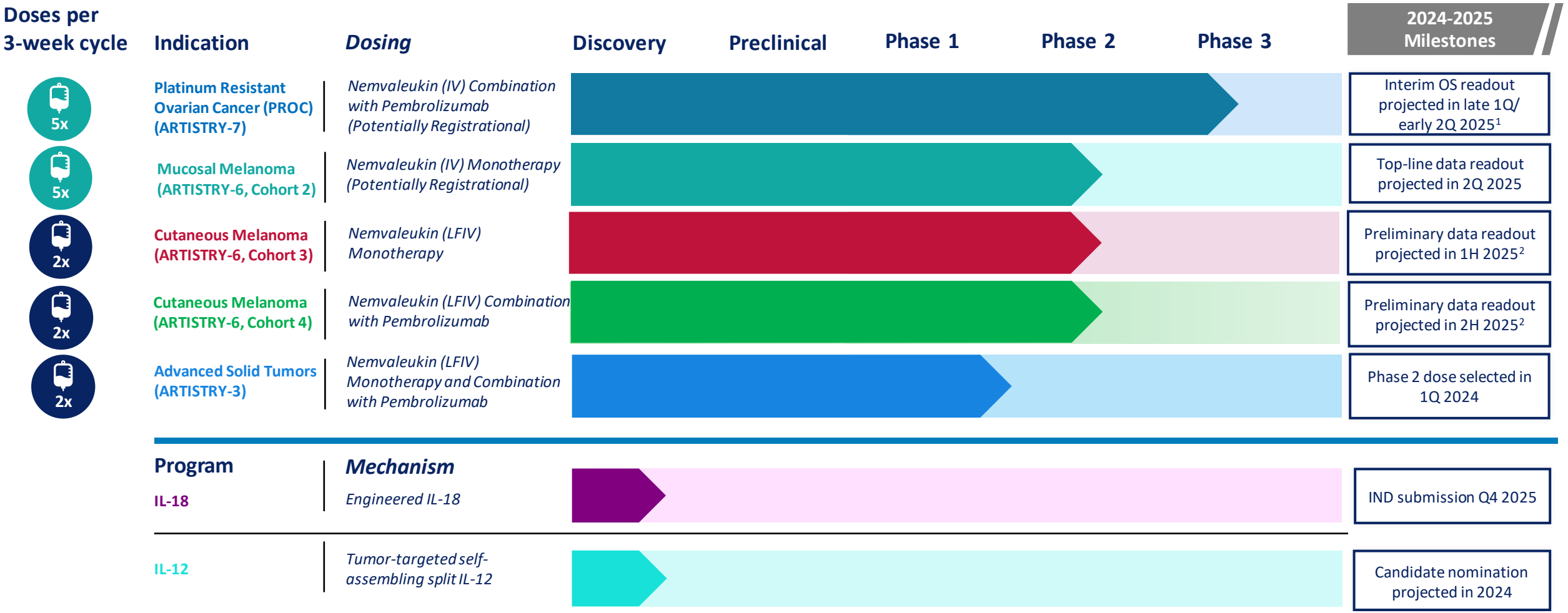
**Scott Jackson**
**MBA – Chairman**

**George Golumbeski**
**PhD**

**Sachiyo Minegishi**
**MBA**

**Caroline Loew**
**PhD**

# Pipeline Overview: 2024-2025 Milestones




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



Abbrev.: **IL**: interleukin; **IV**: intravenous; **LFIV:** less frequent IV dosing; **OS**: overall survival; IND: Investigational New Drug



MURAL ONCOLOGY

SECTION 2:

# NEMVALEUKIN ALFA

MURAL ONCOLOGY

# Nemvaleukin: Engineered to Unlock the Efficacy Potential of the IL-2 Pathway for More Patients

| | |
|---|---|
| **Target with Validated Efficacy:** | **PROLEUKIN©(aldesleukin): proven curative potential in melanoma and RCC**<br>• Extremely durable complete responses<br>• Toxic AE profile requires administration in an acute care setting, severely limits use to the fittest patients |
| **A New Class of Cytokine Therapy:** | **Nemvaleukin: a novel, stable, immediately active fusion protein**<br>• Engineered to selectively expand CD8+ T cells and NK cells while mitigating toxicity<br>• Fusion of alpha sub-unit preferentially binds to beta and gamma receptor complex, hinders binding to trimeric high-affinity receptor |
| **Nemvaleukin's Comprehensive Clinical Dataset:** | **Deep and durable responses in Ph1/2 trial (ARTISTRY 1)**<br>• Durable responses seen with monotherapy in post PD-1 cutaneous and mucosal melanoma<br>• Durable responses, including complete responses, seen in combination therapy with pembrolizumab in heavily pre-treated PROC patients[1]<br>• Manageable AE profile for outpatient administration<br>• Currently in two registrational studies – mono and combination therapy |

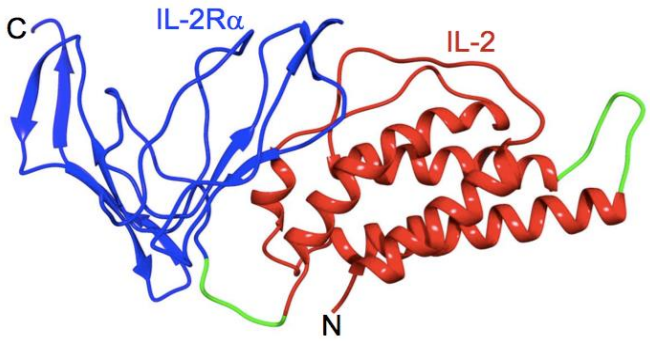
1. Data available on slide 13 of this presentation
2. ARTISTRY-7 (combination therapy), ARTISTRY-6, cohort 2 (monotherapy)



MURAL ONCOLOGY

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

## Nemvaleukin




## Novel Fusion Protein Designed to:

### Maintain Known Efficacy

- ✓ Clear expansion and activation of CD8 T cells
- ✓ Immediately active

### Mitigate Pathway Toxicity

- ✓ Fusion of alpha sub-unit leads to minimal activation of immune-suppressive $T_{regs}$
- ✓ Manageable adverse event profile for outpatient administration

**Other IL-2 Variant Approaches:**

- Shielding
- Masking
- Prodrug
- Pegylation

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

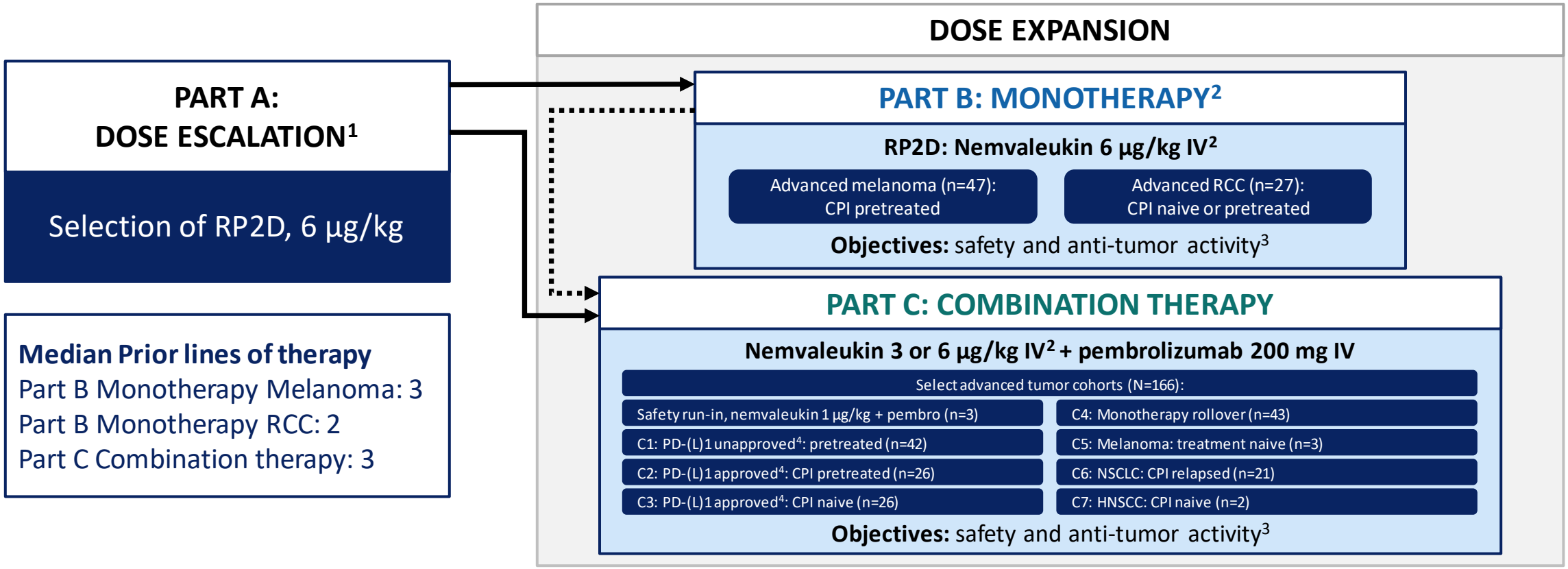


Abbrev: **CPI**: checkpoint inhibitor; **IL-2:** interleukin-2



MURAL ONCOLOGY

# 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

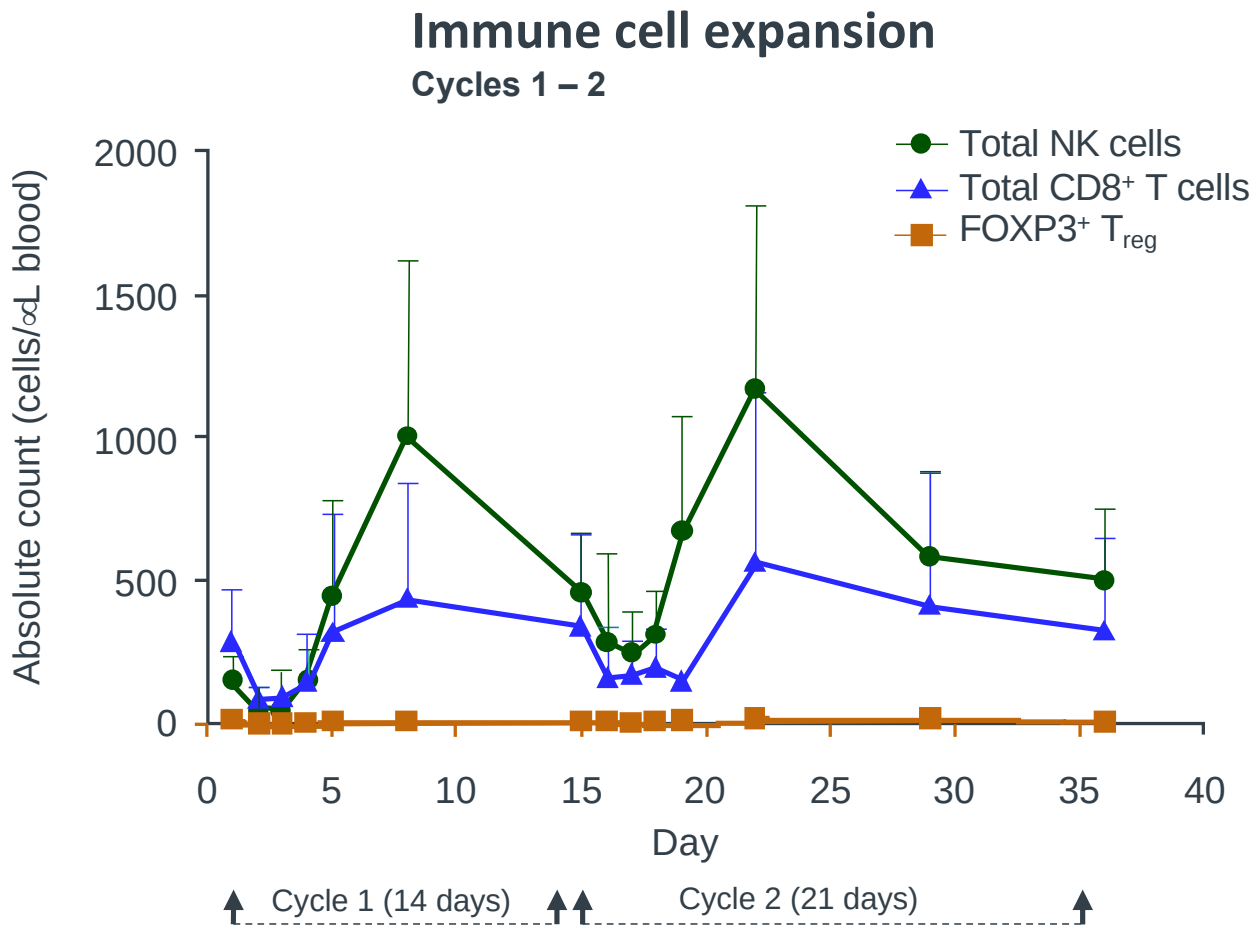


**Abbrev.: C1-7**: Cohorts 1-7; **CPI**: checkpoint inhibitor; **HNSCC**: head & neck squamous cell carcinoma; **IV**: intravenous; **NSCLC**: non-small cell lung cancer; **ORR**: overall response rate; **PD-(L)1**: programmed death (ligand) 1; **RCC**: renal cell carcinoma; **RECIST**: Response Evaluation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



MURAL ONCOLOGY

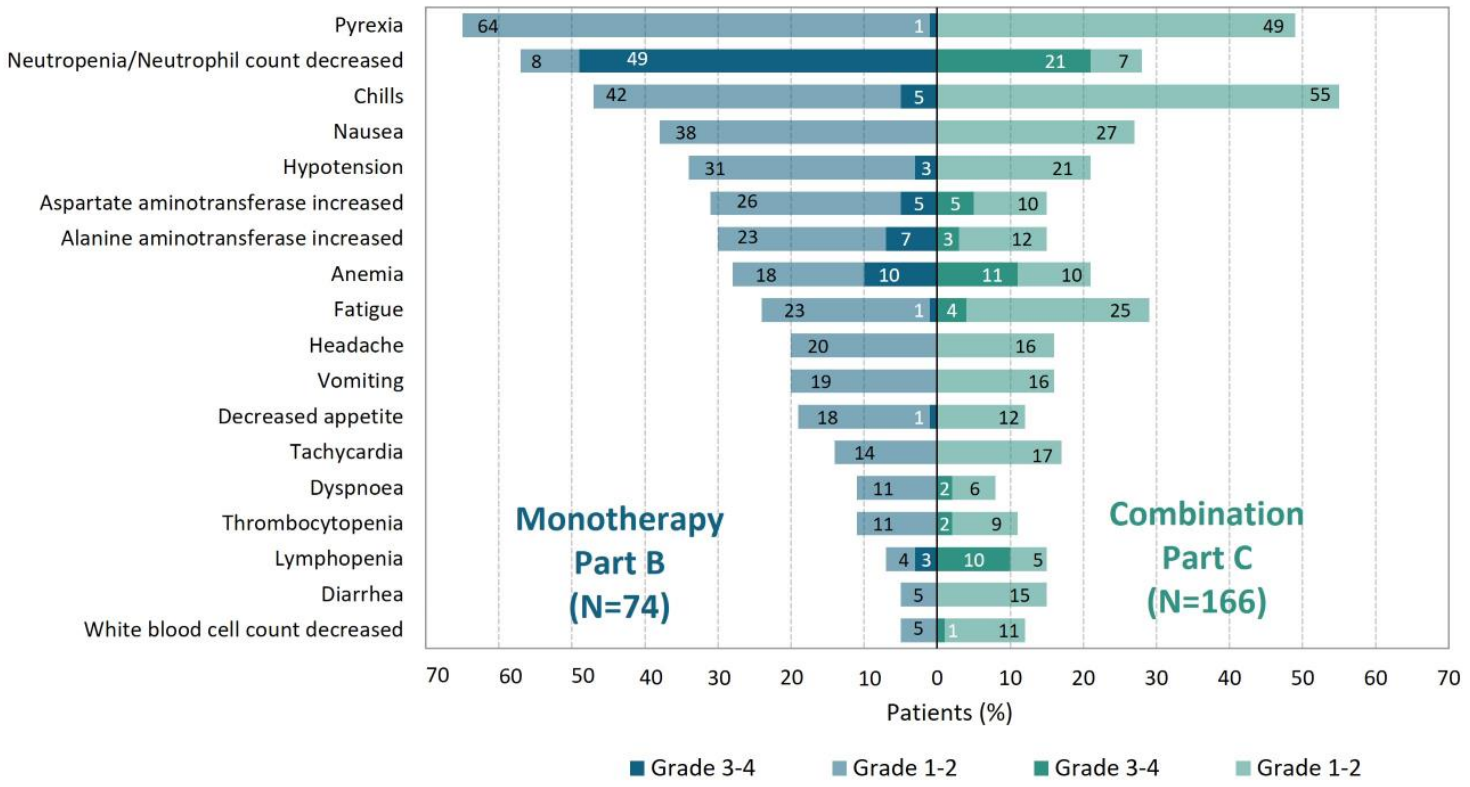
# ARTISTRY-1 Proof of Mechanism: Nemvaleukin Preferentially Expands Cytotoxic CD8+ T Cells and NK Cells While Minimally Expanding $T_{regs}$




Data are from the 6 µg/kg cohort in Part A of ARTISTRY-1. Data are mean + SD (N=12).
Vaishampayan et al. Oral Abstract 2500 presented at ASCO 2022. Abbrev: **NK**: natural killer; **Tregs**: regulatory T cells

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

*Dose expansion: monotherapy (Part B) and combination therapy (Part C)*



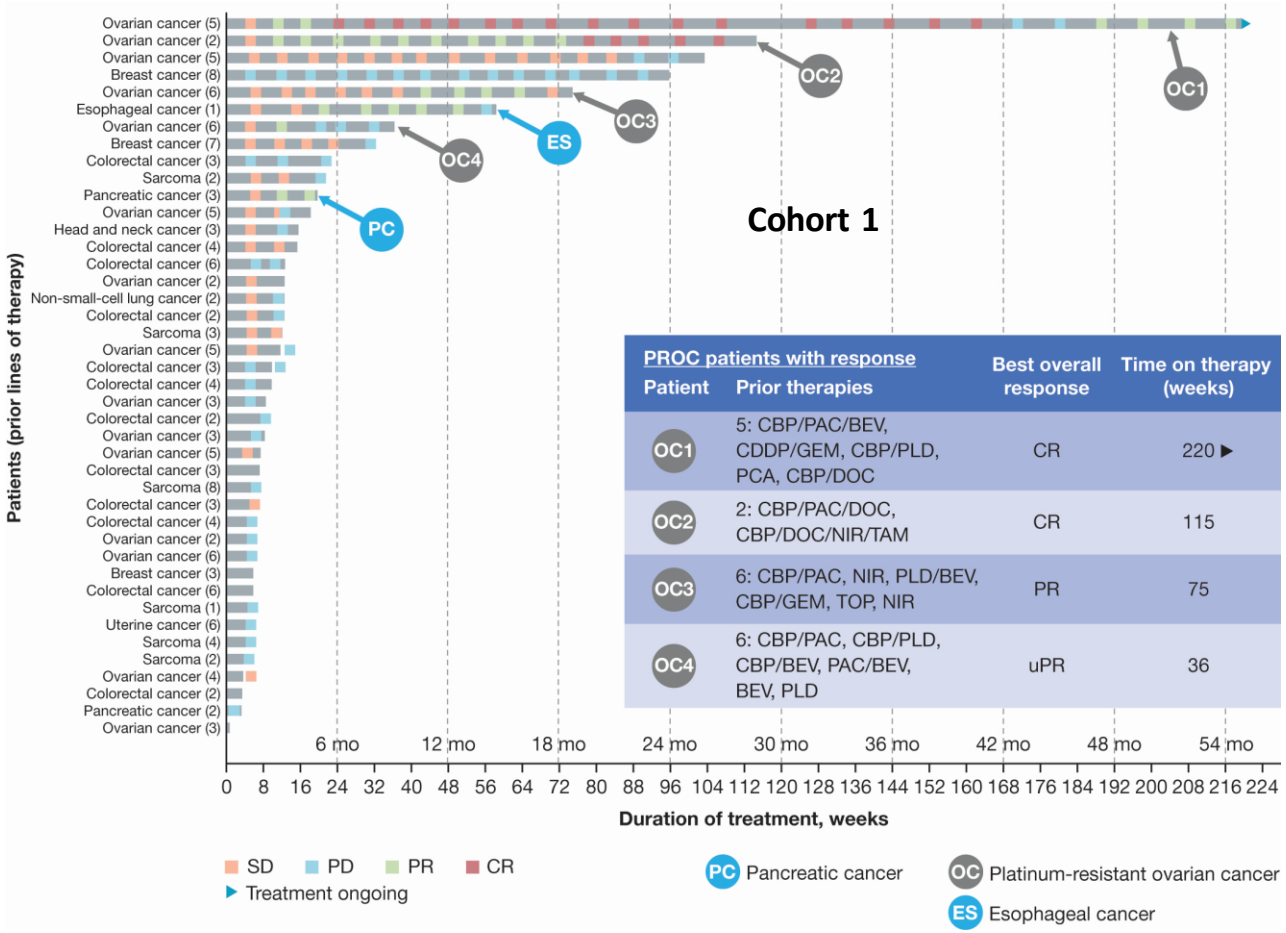

Data as of March 27, 2023

- 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]
  - Not associated with risk of serious infections or febrile neutropenia
- No capillary leak events reported in ART-1
- 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 Gr 1 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 on file.

# 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)* |
| ORR, n (%) | 4 (28.6)* |
| DOR in weeks | 27.6-130.4[1] |

* 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
1. DOR data cut off Sept 27, 2023

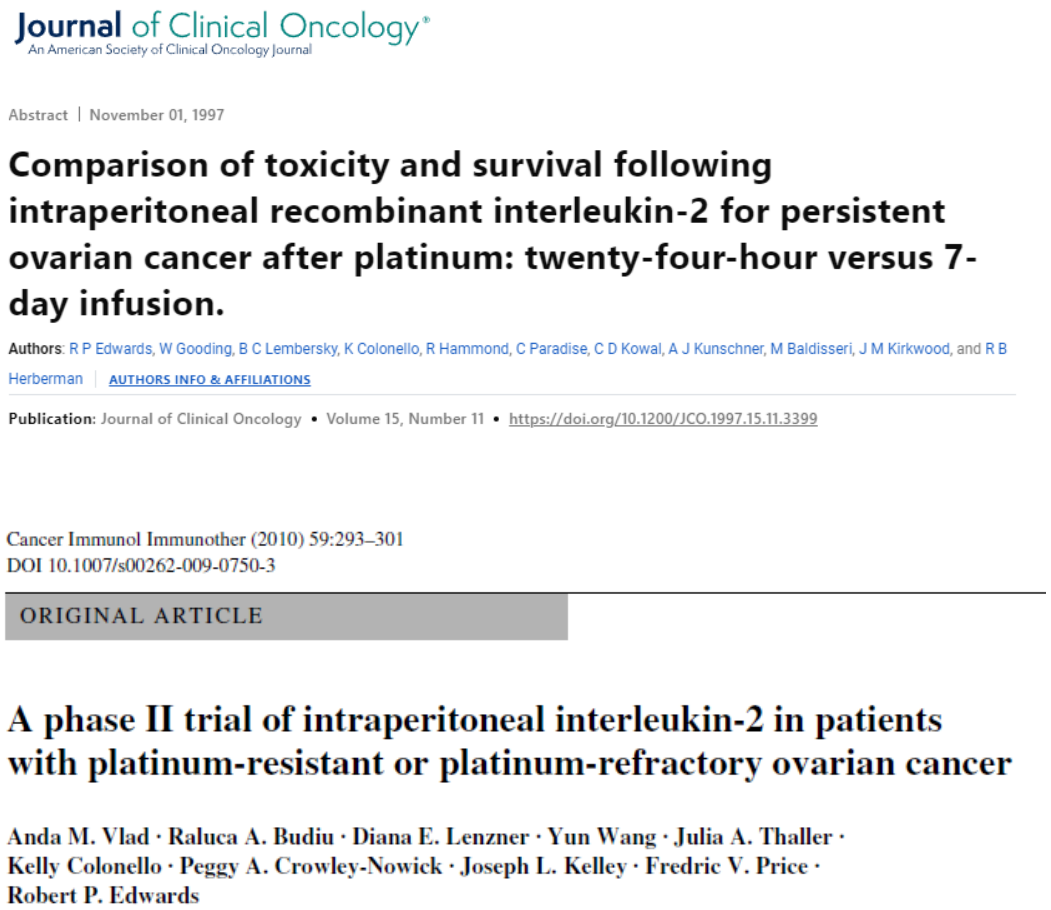


Abbrev.: **BEV**: bevacizumab; **CBP**: carboplatin; **CDDP**: cisplatin; **CR:** complete response; **DOC**: docetaxel; **FDA**: Food and Drug Administration; **GEM**: gemcitabine; **mo**: month; **NIR**: niraparib; **PAC**: paclitaxel; **PCA**: paclitaxel albumin; **PD**: progressive disease; **PD-(L)1**: 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. Data on file.



MURAL ONCOLOGY

# 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



MURAL ONCOLOGY

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

## Investigational Nemvaleukin IV + Pembrolizumab versus Chemotherapy

**Final Enrollment: 456 patients** (vs 448 planned)

Randomization
3:1:1:3
Futility analysis completed for monotherapy arms

### 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

**Arm 1**
Nemvaleukin IV 6 µg/kg + Pembrolizumab[1] IV 200 mg
21-day cycle
Daily IV → 16-day nontreatment period

**Arm 2**
Pembrolizumab[1] IV 200 mg
21-day cycle
20-day nontreatment period

**Arm 3**
Nemvaleukin IV 6 µg/kg
21-day cycle
Daily IV → 16-day nontreatment period

**Arm 4**
Investigator's Choice Single-Agent Chemotherapy

- **PLD IV**, 40 mg/m$^2$ (Day 1 of 28-day cycle)
- **Paclitaxel IV**, 80 mg/m$^2$ (Days 1, 8, 15, and 22 of 28-day cycle)
- **Topotecan IV**, 4 mg/m$^2$ (Days 1, 8, and 15 of 28-day cycle)
- **Gemcitabine IV**, 1000 mg/m$^2$ (Days 1 and 8 of 21-day cycle)

### 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/m$^2$ on Days 1-5 of 21-d cycles
[b] Response per RECIST v1.1
[c] Response per GCIG

1. Pembrolizumab may be administered up to 35 cycles.

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





MURAL ONCOLOGY

# ARTISTRY-7 Interim Analysis Readout Expected Late Q1 or Early Q2 2025

## EVENTS AND STATISTICS

**# of Events:** Protocol specified interim analysis (IA) for overall survival (OS) will occur at 75% of events (~215 of 286 total events)

**Alpha Spend:** Cumulative alpha spend at IA is 1-sided, 0.0096

**Protocol assumptions:** median OS of 10 months for chemotherapy arm and median OS of 14.3 months for Arm 1 (nemvaleukin + pembrolizumab)

**Hazard Ratio:** Maximum hazard ratio for success is 0.727 (a 27.3% reduction in the risk of death[1])

## TIMING

**Events:** ~215 events for interim analysis estimated by late Q4 2024 or early Q1 2025

**Data Readout: OS IA readout in late Q1 or early Q2 2025**

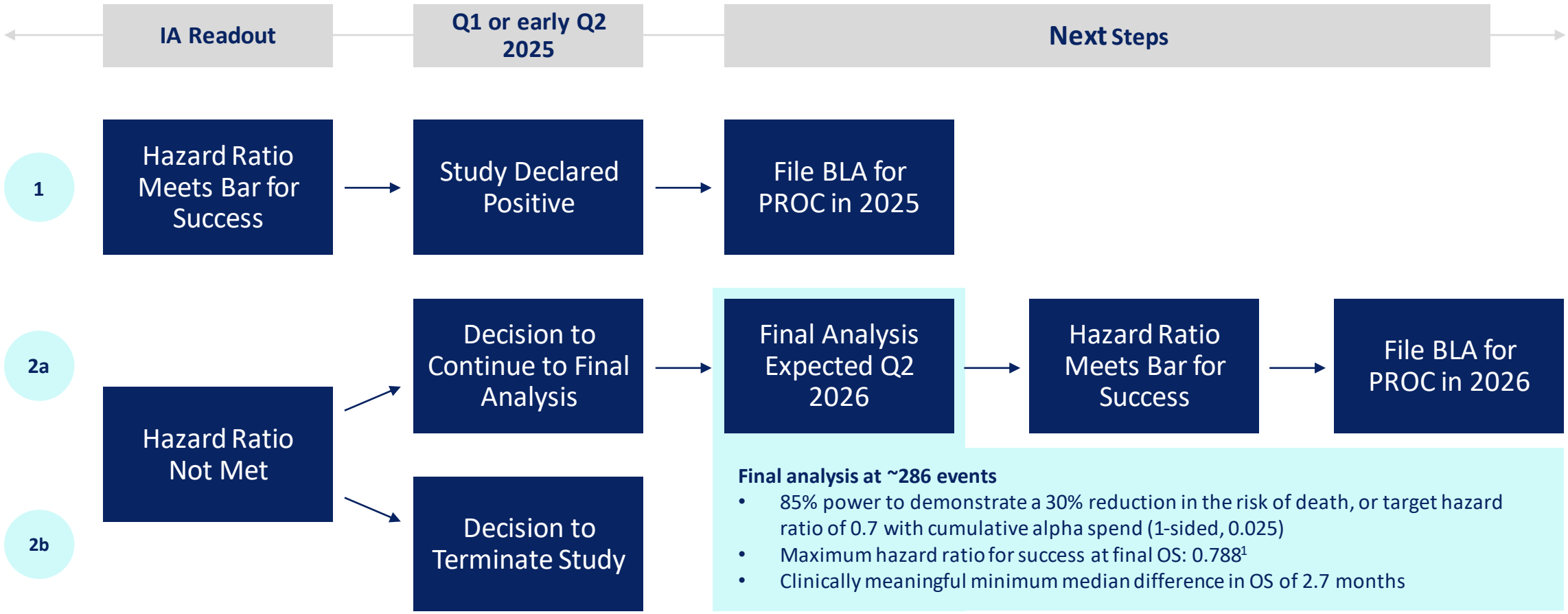
1. Assuming exactly 215 events



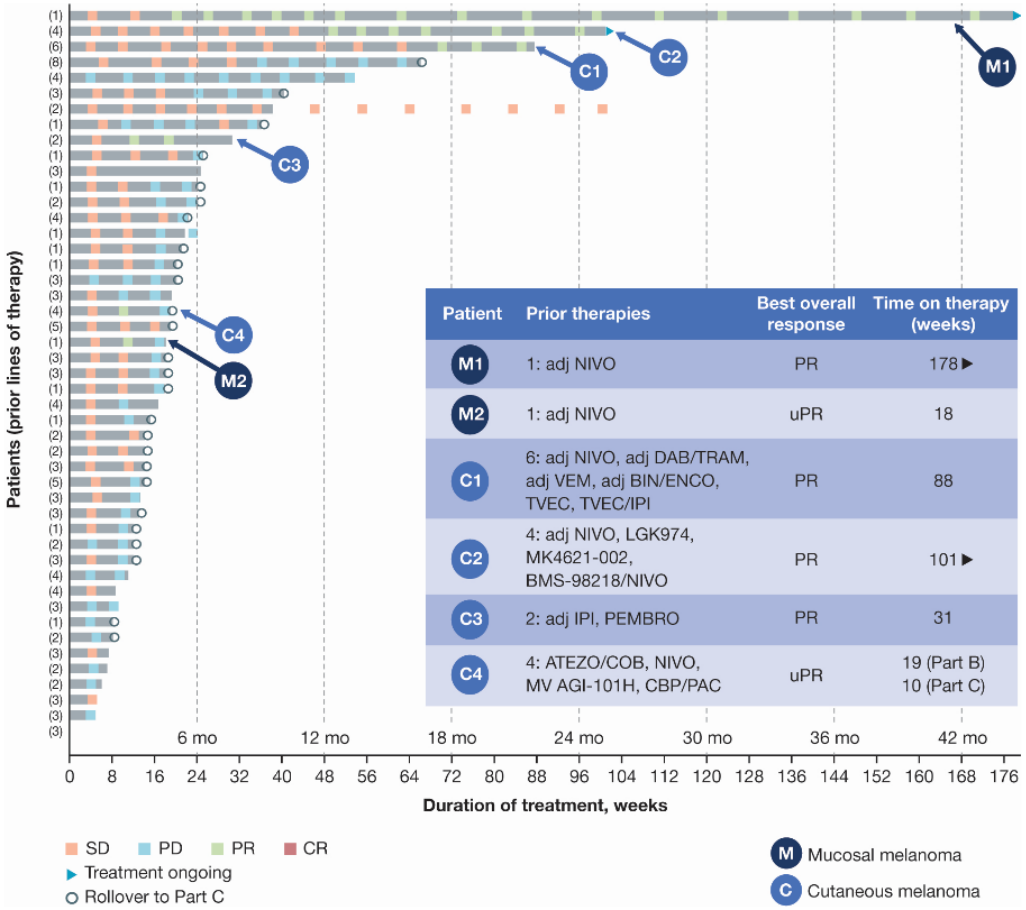


MURAL ONCOLOGY

# ARTISTRY-7 Interim Analysis (IA): Potential Outcomes



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




Responses per RECIST v1.1

| | All[a,b] (n=46) | Mucosal (n=6) |
|---|---|---|
| Best overall response, n (%) | | |
| CR | 0 | 0 |
| PR | 6 (13.0)[c] | 2 (33.3)[d] |
| ORR, n (%) [95% CI] | 6 (13.0) [4.9-26.3][c] | 2 (33.3) [4.3-77.8][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. Data on file.



MURAL ONCOLOGY

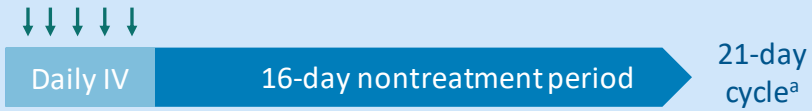
# Cohort 2 of ARTISTRY-6: Phase 2 - Potentially Registrational Trial of Nemvaleukin in Mucosal Melanoma

**Final Enrollment:** 92 patients

## 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 are 21 days[3]

↓ Nemvaleukin dosing

- ARTISTRY-6 also includes Cohorts 1, 3, and 4 which are designed to explore alternative dosing regimens of nemvaleukin, both as a monotherapy and in combination with pembrolizumab, 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





MURAL ONCOLOGY

# ARTISTRY-6 Cohort 2: Data Readout Expected in Q2 2025

- Cohort 2 of ARTISTRY-6 study expected to provide the most robust clinical dataset in advanced mucosal melanoma to date
- Primary analysis will occur when all patients have a minimum follow up of at least 6 months
- **Target response rate: 25%**
  - We believe a response rate of 20-25% would be meaningful for patients and would support discussion with FDA around Biologics License Application (BLA) submission
- Trial designed so that at 25% response rate, lower bound of 95% confidence interval will exceed a 15% response rate
- Intend to discuss data with FDA in advance of BLA submission
  - Potential accelerated approval with confirmatory evidence to be later submitted for conversion to regular approval
  - Regulatory filing may be deferred if ARTISTRY-7 study continues to final analysis, pending the final outcome

Abbrev.: BLA: Biologics License Application





MURAL ONCOLOGY

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


**6 µg/kg; 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


**30 µg/kg; Days 1 and 8 Q3W**
Improved patient-friendly dosing schedule

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

**Cohorts 3 & 4 of ARTISTRY-6**
Phase 2
Cutaneous Melanoma

**Future Nemvaleukin Clinical Trials**


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



MURAL ONCOLOGY

# Cohorts 3 and 4 of ARTISTRY-6: Phase 2 Trial in Melanoma

## Key eligibility criteria[1]

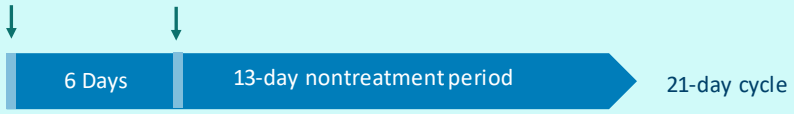
- Unresectable and/or metastatic cutaneous melanoma
- ECOG PS 0-1
- Measurable disease per RECIST v1.1

- Cohort 3 only
  - Patient has received anti–PD(L)-1 ± anti–CTLA-4 or anti-LAG-3 therapy
  - No more than 1 other prior systemic therapy

- Cohort 4 only
  - Prior adjuvant/neo-adjuvant therapy with anti–PD(L)-1 therapy if ≥ 6 mos have elapsed between date of last dose and date of recurrence
  - No prior systemic therapy for unresectable or metastatic disease

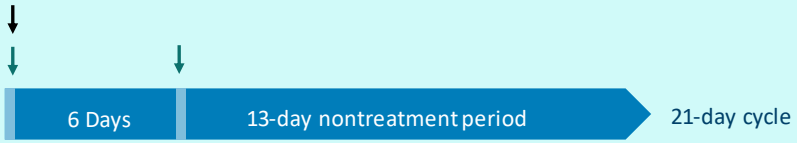
**Cohort 3**
**Cutaneous Melanoma – Monotherapy** (N=30)

Nemvaleukin LFIV 30 µg/kg d1, 8 Q3W




**Cohort 4**
**Cutaneous Melanoma – Combination with Pembro** (N=20)

Nemvaleukin LFIV 30 µg/kg d1, 8 Q3W[2] + Pembrolizumab IV 200 mg




## Key endpoints

- **Primary:** ORR per RECIST v1.1
- **Key secondary:** DOR, PFS, DCR, TTR per RECIST v1.1

Pembrolizumab dosing  Nemvaleukin dosing

1. https://clinicaltrials.gov, NCT04830124
2. Nemvaleukin starting dose will be 30 µg/kg but will allow for de-escalation as necessary per safety data review

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.





MURAL ONCOLOGY

# Focused on Near Term Expansion With Vision Towards Next-Generation IO Opportunity

## Clinical Validation
Initial indications with high unmet need

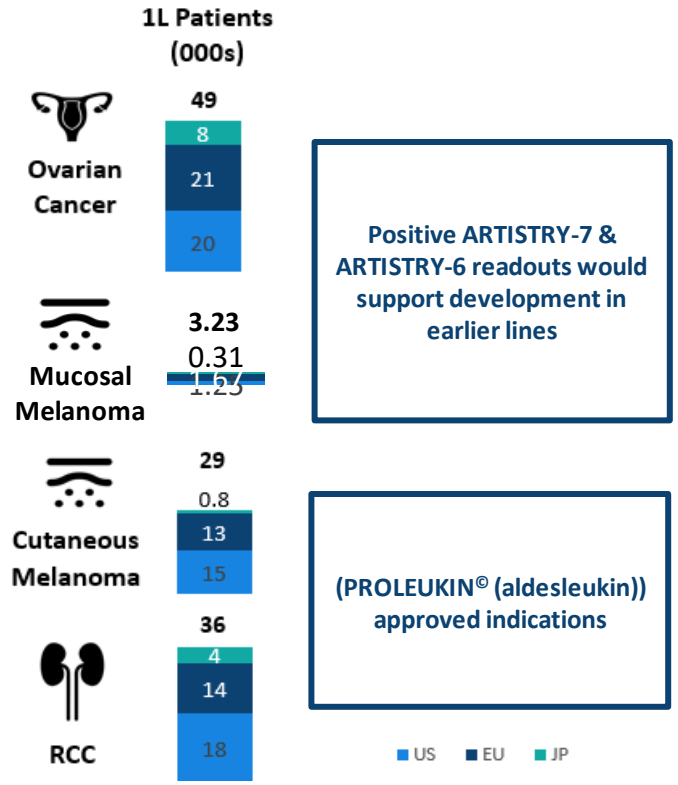
### Platinum-Resistant Ovarian Cancer
13K Patients[1]

- FDA Fast Track Designation
- Potential to be the first immunotherapy option for ovarian patients

### Mucosal Melanoma
2K Patients[1]

- FDA Fast Track and Orphan Drug Designation
- Potential to be first and only approved therapy specific to mucosal melanoma

## Expansion
Larger populations with established clinical rationale

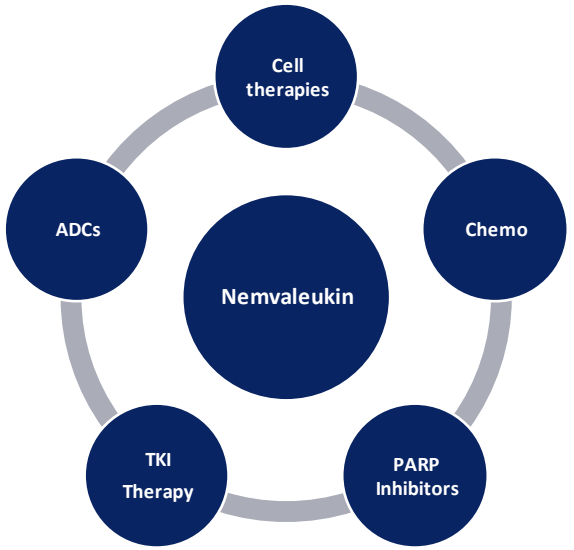



Positive ARTISTRY-7 & ARTISTRY-6 readouts would support development in earlier lines

(PROLEUKIN© (aldesleukin)) approved indications

## Next-Gen IO Backbone
Elevating outcomes / broadening IO patient population

**Biologic rationale for augmenting existing treatment options**




Source: Clarivate Epidemiology; 1) US and EU Patient Populations.

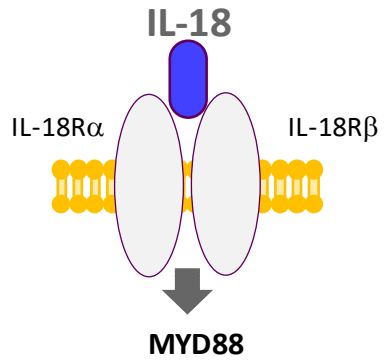
SECTION 3:

# ADDITIONAL PIPELINE PROGRAMS

MURAL ONCOLOGY

# IL-18 is a Potent Stimulator of Innate and Adaptive Immunity, but with Key Limitations

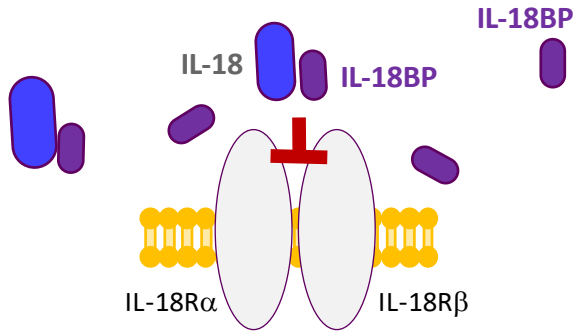
## *IL-18 Attractive Biology*




- **Activates NK cells and antigen-experienced CD8⁺ T cells**
- **Restores activity in dysfunctional T cells**
- **Matures dendritic cells (DCs)**

***Limited Application***

## *IL-18 Challenges*

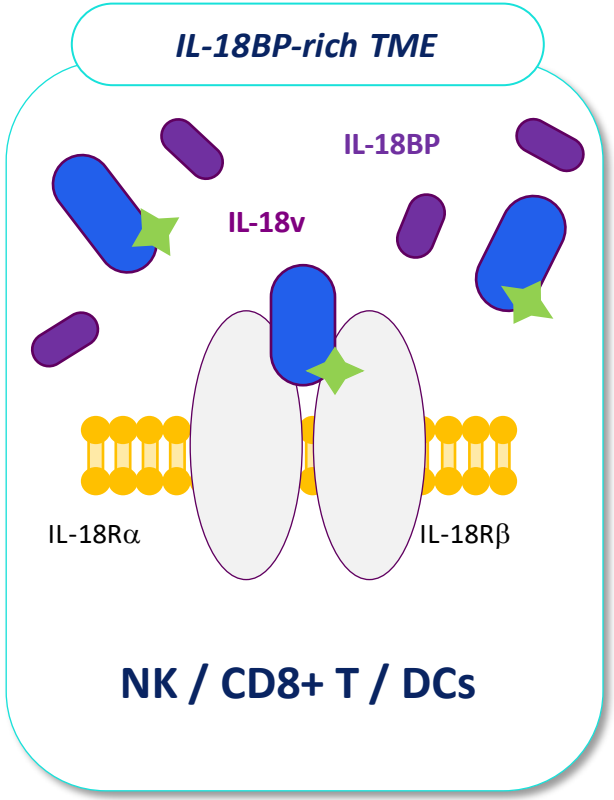



- **IL-18BP overexpressed in the TME**
- **IL-18BP binds strongly to IL-18 minimizing it's signaling**
- **IL-18 rapidly cleared from circulation**

***Suppressed activity***

# Mural's Oncology IL-18: Engineered to Deliver a More Sustained Immune Response

## Mural Solution: Engineer an IL-18 with Optimized Characteristics



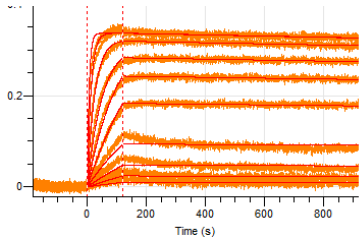

- **Engineer an active IL-18 molecule unaffected by IL-18BP presence**
- **Engineer an IL-18 with an extended half-life**
- **Optimize the IL-18 potency to fit its newly engineered profile**

***Enhanced Anti-Tumor Activity***

# Preclinical Studies Demonstrated Enhanced Pharmacokinetics with an Optimized Potency and Maximal Resistance to IL-18BP Inhibition

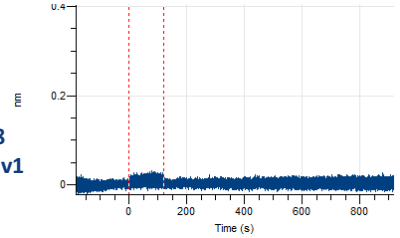
## No Binding of Mural Oncology Variants to IL-18BP

Native HuIL-18 tight binding to IL18-BP

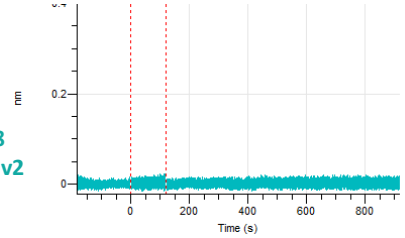



No binding of MOV to IL18-BP

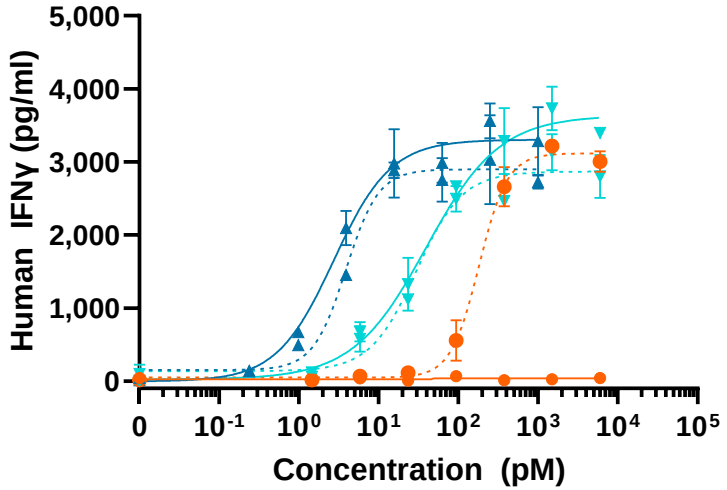
IL-18 huMOv1




IL-18 huMOv2

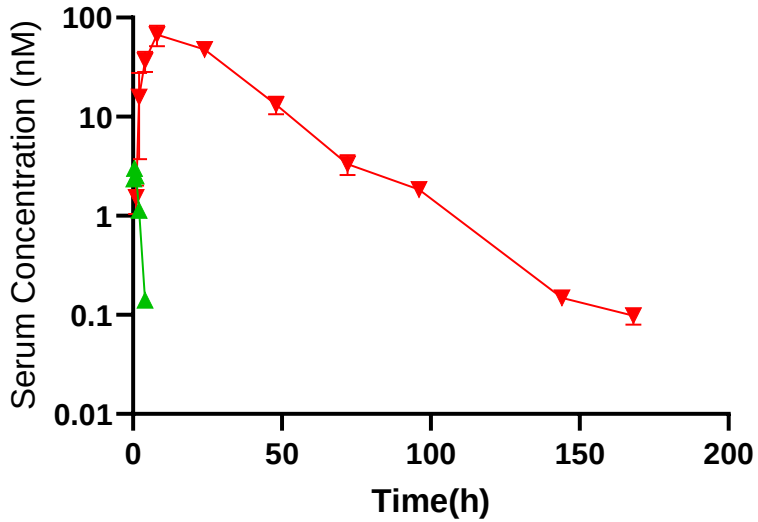



## Broad Range of Potency




**huMOv1/2/3- human Mural Oncology variants**
IL18BP-resistant, half-life enhanced

## Enhanced Pharmacokinetics

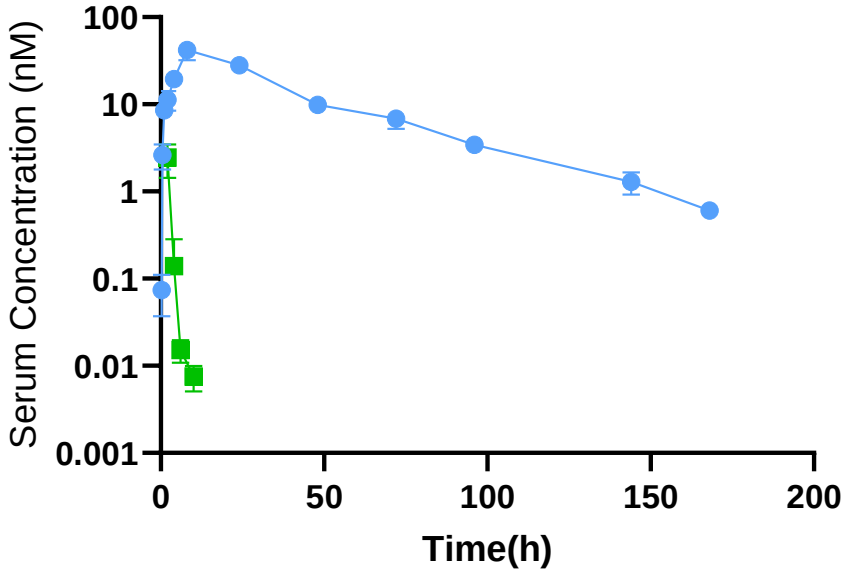





MURAL ONCOLOGY

# Mural's Approach Achieves Intended Half-Life and Associated Pharmacodynamics Effects

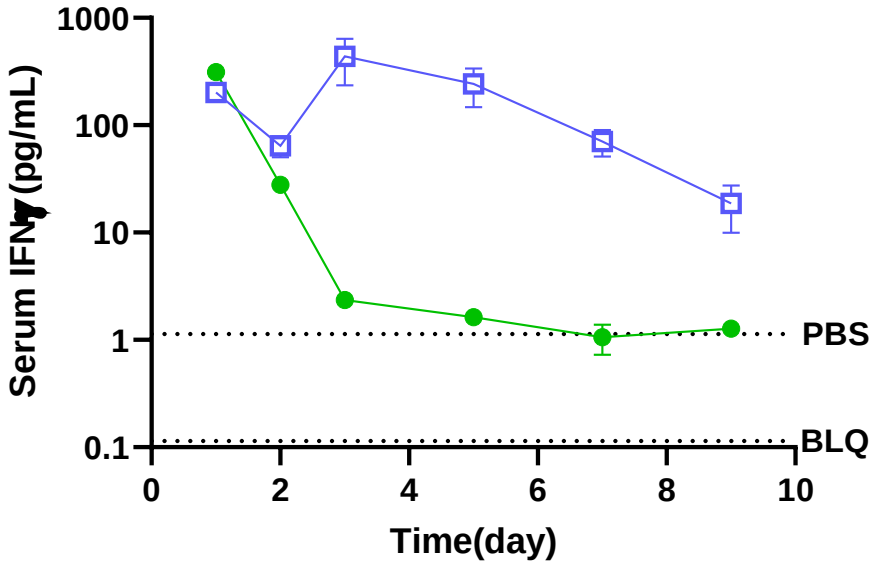
## Enhanced Pharmacokinetic




Naked mouse tool variant

muMOv1

## Extended Pharmacodynamic




Naked mouse tool variant

muMOv1

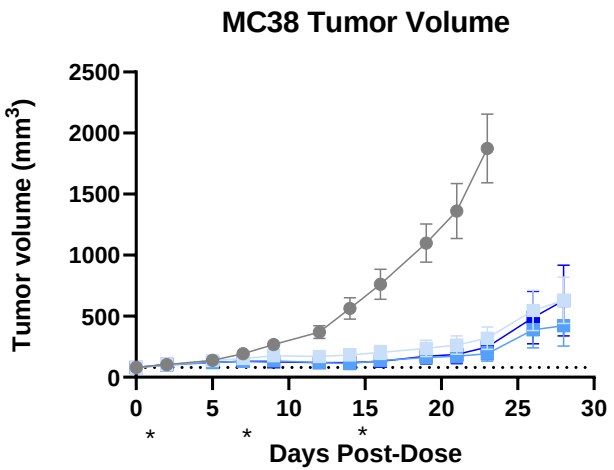
**muMOv1-mouse Mural Oncology variant**
IL18BP-resistant, half-life enhanced

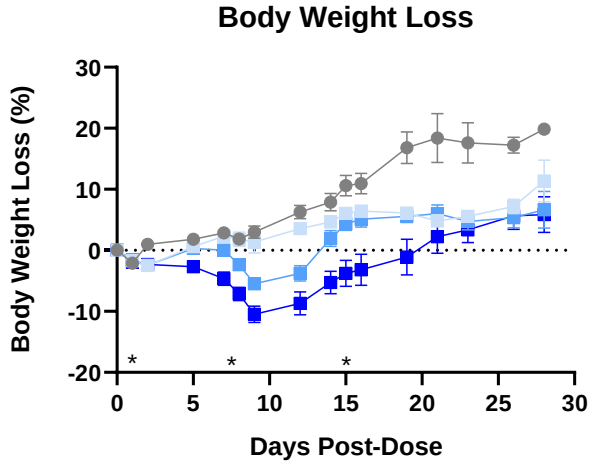


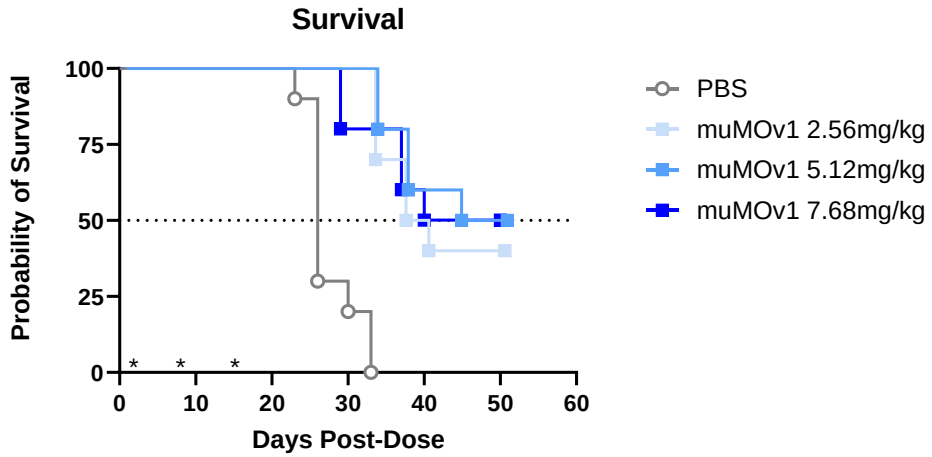


MURAL ONCOLOGY

# Complete Responses and Survival Improvement Seen in Mural's IL-18 Mouse Ortholog Variant




| Agent | Dose (mg/kg) | % TGI* Day 21 | Complete Response Day 50 | Probability of Survival Day 50 |
|---|---|---|---|---|
| muMOv1 | 2.56 | 86% | 2/10 | 40% |
| muMOv1 | 5.12 | 93% | 4/10 | 50% |
| muMOv1 | 7.68 | 92% | 5/10 | 50% |

**muMOv1-** IL18BP-resistant, half-life enhanced mouse ortholog of Mural human variant

***%TGI = % tumor growth inhibition, calculated before 1st animal in vehicle reached endpoint**

The combination of IL-18BP resistance and half-life enhancement achieved desired effect





MURAL ONCOLOGY

# Mural at a Glance

Phase 2/3

## Late-Stage Trials:

- ✓ **Fully enrolled** for ARTISTRY-7 (Phase 3, PROC) and ARTISTRY-6 cohort 2 (Phase 2, mucosal melanoma)
- ✓ Ongoing discussions with FDA on ARTISTRY-6 potential **confirmatory evidence package**
- ✓ RP2D for **next generation dosing schedule** underway in ARTISTRY-6, cohorts 3 & 4 (phase 2, cutaneous melanoma )

## 2025 CATALYSTS:

- ➢ **Late Q1/Early Q2:** Interim OS for ARTISTRY-7[1]
- ➢ **Q2:** TLR Cohort 2 of ARTISTRY-6
- ➢ **1H:** PDR Cohort 3-mono of ARTISTRY-6 (Phase 2, CM)[2]
- ➢ **2H:** PDR Cohort 4-combo of ARTISTRY-6 (Phase 2, CM)[2]

## Preclinical Assets:

**4Q 2024:** Candidate nominations for IL-18 and IL-12
**4Q 2025:** IL-18 IND submission

## Cash Position:

**Cash runway into 4Q 2025**

## Commercial Opportunity:

Significant opportunity in 2 indications with **limited available therapies** and planned indication expansion

1. Subject to 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; **PDR**: preliminary data readout; **PROC**: platinum resistant ovarian cancer; **RP2D**: recommended phase 2 dose; **TLR**: topline results



MURAL ONCOLOGY

# THANK YOU!

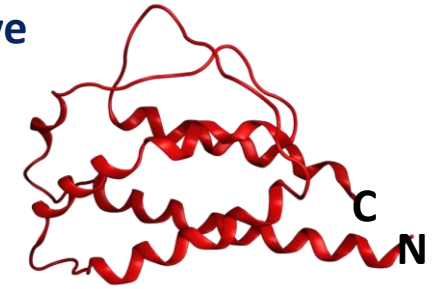
MURAL ONCOLOGY

# APPENDIX

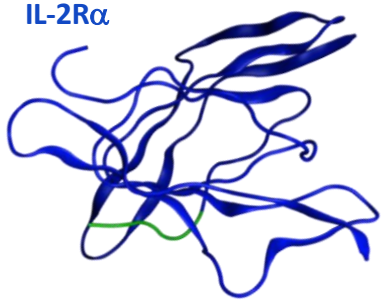
MURAL ONCOLOGY

# Nemvaleukin Design Details: A New Class of Engineered Fusion Protein Targeting IL-2 Pathway

**Native IL-2:**

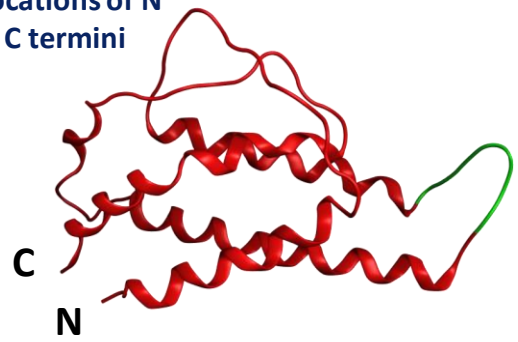



IL-2Rα



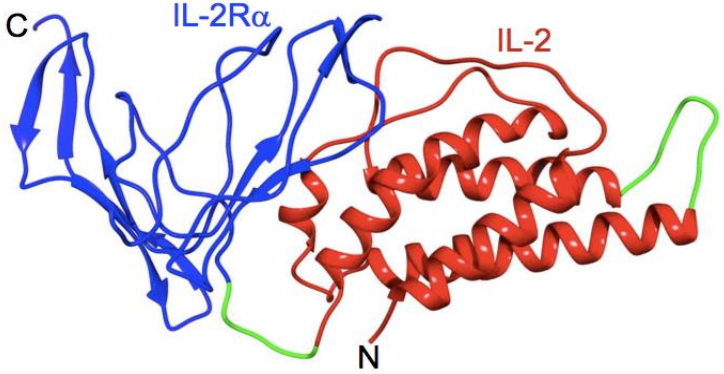
+

New locations of N and C termini




**Nemvaleukin:**

=




- Native component of IL-2 receptor complex directly blocks α component of high affinity IL-2R
- Minimal alteration to IL-2 sequence maintains IL-2's structure and allows for appropriate placement of α subunit

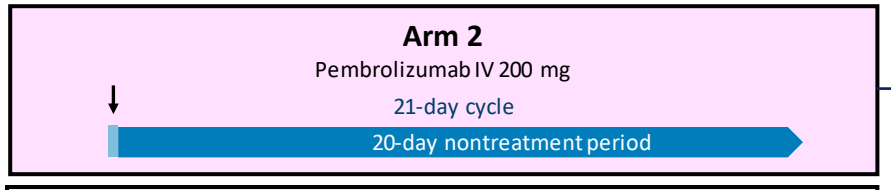


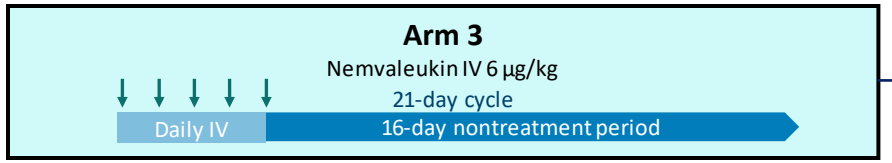


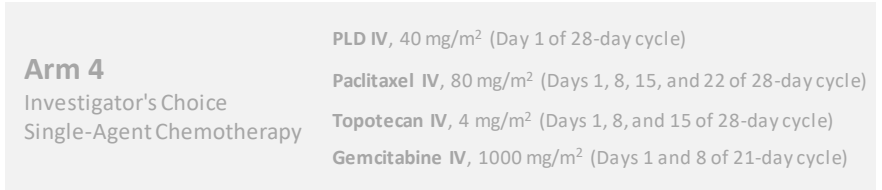
MURAL ONCOLOGY

# ARTISTRY-7: Futility Criteria for Monotherapy Arms

## Smaller Single Agent Arms to Assess Contribution of Components


**Futility criteria for Arm 2:**

- Based on Keynote-100 trial, where single agent pembro was evaluated in 376 patients with PROC with a response rate of 8%
- Futility in ARTISTRY-7 trial defined as <2 confirmed complete or partial responses in the first 12 patients enrolled
- **This arm was closed to further enrollment for futility in August 2023 after enrolling 27 patients**

**Futility criteria for Arm 3:**

- Based on two phase 2 trials using different doses and schedules of aldesleukin with consistent response rates of approx. 25%, including some patients with durable CRs[1]
- At least 1 patient among first 24 enrolled to achieve ORR or SD for at least 3 months needed to continue enrollment
- **Nemvaleukin single agent arm met the threshold to continue and enrolled a total of 55 patients**

1. Edwards et al. "Comparison of toxicity and survival following intraperitoneal recombinant interleukin-2 for persistent ovarian cancer after platinum: twenty-four-hour versus 7-day infusion." *Journal of Clinical Oncology*, November 1, 1997; Vlad et al. "A phase II trial of intraperitoneal interleukin-2 in patients with platinum-resistant or platinum-refractory ovarian cancer." *Cancer Immunology and Immunotherapy*. February 2010.



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



MURAL ONCOLOGY