UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 8-K

Current Report Pursuant to
Section 13 or 15(d) of the
Securities Exchange Act of 1934

Date of Report (Date of Earliest Event Reported): September 26, 2024

Mural Oncology plc

(Exact name of Registrant as Specified in Its Charter)

Ireland	**001-41837**	**98-1748617**
(State or Other Jurisdiction of Incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**
10 Earlsfort Terrace **Dublin 2, D02 T380, Ireland** **(Address of Principal Executive Offices)**		**Not Applicable** **(Zip Code)**

Registrant's Telephone Number, Including Area Code: +353-1-905-8020

Not Applicable
(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instructions A.2. below):

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Ordinary Shares, nominal value $0.01	MURA	The Nasdaq Global Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01. Regulation FD Disclosure.

On September 26, 2024, Mural Oncology plc (the "Company") will hold its previously announced "Investor Day" event beginning at 10:00 a.m. ET. During the event, representatives of the Company will, among other things, discuss insights on the design of the Company's late-stage clinical trials of nemvaleukin alfa, its investigational, engineered interleukin-2 cytokine, provide an update on expected timing for anticipated data readouts and other milestones and provide an overview of its interleukin-18 program. A copy of the press release relating to the Investor Day event is attached hereto as Exhibit 99.1 and a copy of the presentation slides to be used by the Company during the Investor Day event and webcast is attached hereto as Exhibit 99.2, both of which are incorporated by reference herein. A live webcast of the Investor Day event may be accessed by visiting the Investors & News section of the Company's website at https://ir.muraloncology.com/events-and-presentations. A recording of the webcast will also be available on the Company's website after the event. The information contained in, or that can be accessed through, the Company's website is not a part of this filing.

The information contained under this Item 7.01 in this Current Report on Form 8-K, including Exhibit 99.1 and Exhibit 99.2, is being furnished herewith and shall not be deemed to be "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section, nor shall such information be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as expressly set forth by specific reference in such a filing.

Item 9.01 Financial Statements and Exhibits

(d) Exhibits

Exhibit No.	Description
99.1	Press release issued by Mural Oncology plc on September 26, 2024.
99.2	Investor Day Presentation dated September 26, 2024.
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Mural Oncology plc

Dated: September 26, 2024

By: /s/ Maiken Keson-Brookes

Name: Maiken Keson-Brookes

Title: Chief Legal Officer

FOR IMMEDIATE RELEASE

Mural Oncology's First Virtual Investor Day to Highlight Late-Stage Clinical Progress

Key data readouts for the company's late-stage, potentially registrational trials of nemvaleukin are expected in late Q1/early Q2 2025 for platinum-resistant ovarian cancer and Q2 2025 for mucosal melanoma

Management team to provide additional information not previously disclosed related to nemvaleukin study design, statistical assumptions, and study execution

Clinicians to discuss treatment landscape of platinum-resistant ovarian cancer and mucosal melanoma, two indications with limited treatment options and poor outcomes for patients

IND submission for Mural's IL-18 program planned forQ4 2025

WALTHAM, Mass and DUBLIN – September 26, 2024 – Mural Oncology plc (Nasdaq: MURA), a clinical-stage immuno-oncology company developing novel, investigational engineered cytokine therapies designed to address areas of unmet need for patients with a variety of cancers, will host a virtual Investor Day today beginning at 10 a.m. ET. Mural leadership will provide new clinical insight into the trial design, statistical assumptions, and progress of the company's late-stage trials of nemvaleukin.

"Mural has the most advanced IL-2 program currently in development and we have made significant progress this year. We have a great deal of conviction around nemvaleukin, which is engineered to unlock the efficacy potential of high dose IL-2 for more patients, and we are pleased to share more details around our study designs and assumptions during today's Investor Day," said Caroline Loew, Ph.D., CEO of Mural Oncology. "There has also been significant interest in our IL-18 program and we announced today that we plan to submit an IND to the FDA for this program in Q4 2025. Together we believe these programs have the potential to be the next wave of much needed treatment options for cancer patients."

ARTISTRY-7:
ARTISTRY-7 is a potentially registrational phase 3 trial comparing the combination of nemvaleukin and pembrolizumab versus investigator's choice single agent chemotherapy in heavily pre-treated patients with platinum-resistant ovarian cancer (PROC), with a primary endpoint of overall survival (OS). Secondary endpoints include progression free survival, overall response rate, disease control rate, duration of response, time to response, CA-125 response, and treatment emergent adverse events. This four-arm trial also contains two smaller monotherapy arms to assess contribution of components.

PROC is an area of high unmet need, with few effective treatment options and poor survival. Nemvaleukin for the treatment of PROC has received Food & Drug Administration (FDA) Fast Track Designation.

Enrollment is complete, with a total of 456 patients (versus 448 planned), and approximately 187 patients in each of the two experimental arms.

Futility analyses are complete for both monotherapy arms:
Pembrolizumab (arm 2):

- Predetermined analysis criteria were based on Keynote-100 trial, where single agent pembrolizumab was evaluated in 376 patients with PROC with a response rate of 8%.
- Futility in this arm of ARTISTRY-7 was defined as fewer than two 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.

Nemvaleukin (arm 3):
- Predetermined futility criteria were based on two historical phase 2 trials using different doses and schedules of aldesleukin, an approved high-dose IL-2, that showed consistent response rates of approximately 25%, including some patients with durable complete responses. [1]
- Futility criteria for this nemvaleukin single arm required at least one patient among the first 24 enrolled to achieve an objective response or stable disease for at least three months to continue enrollment.
- The nemvaleukin single arm met this threshold to continue and ultimately enrolled 55 patients.

No statistical comparisons will be performed on the pembrolizumab and nemvaleukin monotherapy arms; all analyses of these two arms will be descriptive.

ARTISTRY-7 Overall Survival Expectations and Rationale
Based on benchmarking against prior phase 3 trials in PROC, which had different eligibility criteria regarding the number of prior therapies, and the eligibility criteria of ARTISTRY-7 which allow for up to five prior lines of therapy in the platinum-resistant or refractory setting, protocol assumptions are:
- A median Overall Survival (OS) of 10 months for the chemotherapy control arm.
- A median OS of 14.3 months for the nemvaleukin plus pembrolizumab experimental arm.

ARTISTRY-7 Events and Statistics:
- Protocol specific **interim analysis for OS** will occur at 75% of OS events (~215 of 286 total OS events).
- **Cumulative alpha spend** at interim analysis is 1-sided, 0.0096.
- **Maximum hazard ratio** for success at the interim analysis is 0.727 (a 27.3% reduction in the risk of death), assuming exactly 215 OS events.

ARTISTRY-7 Timing:
- With enrollment complete, the OS events required for interim analysis are estimated to occur by late Q4 2024 or early Q1 2025.
- Mural expects the interim analysis data readout to be available in late Q1 or early Q2 2025.
- If the hazard ratio meets the bar for success, the study will be declared positive and the company will plan to file a Biologics License Application (BLA) in 2025.

[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.

- If the target hazard ratio is not met, the company may decide to continue to final analysis at approximately 286 OS events, or it may decide to terminate the study.

ARTISTRY-6, Cohort 2:
ARTISTRY-6 cohort 2 is a potentially registrational single arm study of single agent nemvaleukin in patients with unresectable or metastatic mucosal melanoma. The trial's primary endpoint is overall response rate evaluated per RECIST 1.1 by an independent central radiology review. Secondary endpoints include duration of response, time to response, disease control rate, progression-free survival, and safety.

Mucosal melanoma is a rare subtype of melanoma with poor prognosis and currently no approved treatment options. Nemvaleukin for the treatment of mucosal melanoma has received both FDA Fast Track Designation and Orphan Drug Designation.

Enrollment in this study is complete with 92 patients enrolled.

ARTISTRY-6, Cohort 2 Response Rate Assumptions and Rationale:
The target response rate is 25%. At this target, the lower bound of the 95% confidence interval will exceed a 15% response rate.

Mural believes that in this rare and highly aggressive tumor with poor outcomes even in the first line setting, demonstrating durable responses with a response rate of 20-25% would be meaningful for patients, and would support a discussion with the FDA regarding a potential BLA submission and potential accelerated approval.
A potential accelerated approval would require confirmatory evidence to be agreed with and later submitted to the FDA for conversion to a regular approval. Discussions with FDA on a potential confirmatory evidence package are ongoing.

ARTISTRY-6 Timing:
- The primary analysis will occur when all patients have a minimum follow-up of at least six months. In order to ensure adequate follow-up on all patients, Mural anticipates that the top-line readout will occur in the second quarter of 2025.
- Potential accelerated approval with confirmatory evidence to be later submitted for conversion to regular approval.
- Regulatory filing may be deferred if the ARTISTRY-7 study continues to final analysis, pending the final outcome.

Mural Oncology's IL-18 Program:

Mural plans to nominate a development candidate for its IL-18 program by the end of 2024 and intends to submit an Investigational New Drug (IND) Application to the FDA in Q4 2025.

Mural Investor Day Webcast Details:
Mural's management team will be joined by three clinicians on the webcast to discuss the treatment landscape for PROC and mucosal melanoma, as well as nemvaleukin's clinical proof of concept data.

The live webcast will begin at 10 a.m. followed by a Question & Answer session. To join the webcast, please visit https://ir.muraloncology.com/events-and-presentations.

A replay of the webcast will be available shortly after the conclusion of the meeting.

About Mural Oncology
Mural Oncology is leveraging its novel protein engineering platform to develop cytokine-based immunotherapies for the treatment of cancer. By combining our expertise in cytokine biology and immune cell modulation and our protein engineering platform, we are developing medicines to deliver meaningful and clinical benefits to people living with cancer. Our mission is to broaden the potential, and reach, of cytokine-based immunotherapies to improve the lives of patients. Our lead candidate, nemvaleukin, is currently in potentially registrational trials in mucosal melanoma and platinum-resistant ovarian cancer reading out in the first half of 2025. Mural Oncology has its registered office in Dublin, Ireland, and its primary facilities in Waltham, Mass. For more information, visit Mural Oncology's website at www.muraloncology.com and follow us on LinkedIn and X.

About Nemvaleukin
Nemvaleukin alfa (nemvaleukin) is a novel, engineered cytokine designed to leverage antitumor effects of the IL-2 pathway while mitigating the hallmark toxicities that limit its use. Nemvaleukin selectively binds to the intermediate-affinity IL-2 receptor (IL-2R) and is sterically occluded from binding to the high-affinity IL-2R. Because of this molecular design, nemvaleukin treatment leads to preferential expansion of antitumor CD8+ T cells and natural killer cells, with minimal expansion of immunosuppressive regulatory T cells. Nemvaleukin is currently being evaluated in two potentially registrational late-stage trials.

About Mural Oncology's IL-18 Program
IL-18 is a potent immune-stimulating cytokine, but its efficacy is blunted by IL-18 binding protein (IL-18BP), a high affinity decoy receptor that binds to, and neutralizes, IL-18, thereby rendering it ineffective. Native IL-18's potency is also limited by its short half-life. Mural Oncology's novel approach to protein engineering is designed to mitigate these issues. First, Mural introduced mutations to IL-18 that eliminate binding to IL-18BP while minimally impacting the native IL-18 structure. Second, it fused IL-18 to protein scaffolds which extend the half-life and increase IL-18's exposure. Together, these have demonstrated more durable immunological effect in preclinical studies. Mural intends to nominate a development candidate for its IL-18 program by the end of this year and file an IND submission by the end of 2025.

Forward-Looking Statements
Statements contained in this press release regarding matters that are not historical facts are "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. Because such statements are subject to risks and uncertainties, actual results may differ materially from those expressed or implied by such forward-looking statements. Such statements include, but are not limited to, statements regarding: the company's pipeline and development programs, including the expected timing of clinical updates from the ARTISTRY-6 and ARTISTRY-7 trials, the expected timing of preclinical updates, candidate nomination, and IND submission, including with respect to the Company's IL-18 program, the potential of the company's product candidates and programs to address unmet medical needs, and the continued progress of its pipeline and programs. Any forward-looking statements in this press release are based on management's current expectations of future events and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in or implied by such forward-looking statements. Risks that contribute to the uncertain nature of the forward-looking statements 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; that 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 may make adverse decisions regarding the company's product candidates; and those other risks and uncertainties set forth 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 June 30, 2024 and in subsequent filings the company may make with the SEC. All forward-looking statements contained in this press release speak only as of the date of this press release. The company anticipates that subsequent events and developments will cause its views to change. However, the company undertakes no obligation to update such forward-looking statements to reflect events that occur or circumstances that exist after the date of this press release, except as required by law.

Contact:
Katie Sullivan
katie.sullivan@muraloncology.com

Exhibit 99.2

2024 VIRTUAL INVESTOR DAY: CLINICAL INSIGHTS & CLINICIAN DISCUSSION

September 26, 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; the potential patient populations and market for the indications that the Company is pursuing; 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; 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 June 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.

Highly Experienced Late-Stage Oncology Team

Executive Team

Caroline Loew, PhD
CEO

glympse bio · Bristol Myers Squibb · MERCK · PhRMA

Adam Cutler
CFO

32 BIO · tem · Arbutus BIOPHARMA · CREDIT SUISSE

Vicki Goodman, MD
CMO

EXELIXIS · Bristol Myers Squibb · MERCK · FDA

Maiken Keson-Brookes
CLO

RubiusTherapeutics · synlogic · uniQure · Biogen

Board of Directors

Francis Cuss
MB, BChir, FRCP

Bristol Myers Squibb · GSK · Schering-Plough

Benjamin Hickey
MBA

RayzeBio · MIRATI THERAPEUTICS · Halozyme · Bristol Myers Squibb

Scott Jackson
MBA – Chairman

Celator Pharmaceuticals · Lilly · SB SmithKline Beecham · ImClone Systems Incorporated

George Golumbeski
PhD

GRAIL · Celgene · NOVARTIS

Sachiyo Minegishi
MBA

RECTIFY · AKOUOS · bluebirdbio · genzyme

Caroline Loew
PhD

glympse bio · Bristol Myers Squibb · MERCK · PhRMA

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

Nemvaleukin: Engineered to unlock the efficacy potential of High Dose IL-2 for more patients

High dose (HD) IL-2 (PROLEUKIN©/aldesleukin) has proven curative potential in melanoma and RCC

- Extremely durable complete responses
- However toxic AE profile requires administration in an acute care setting, and severely limits use to the fittest patients

Nemvaleukin is a novel, stable, immediately active fusion protein

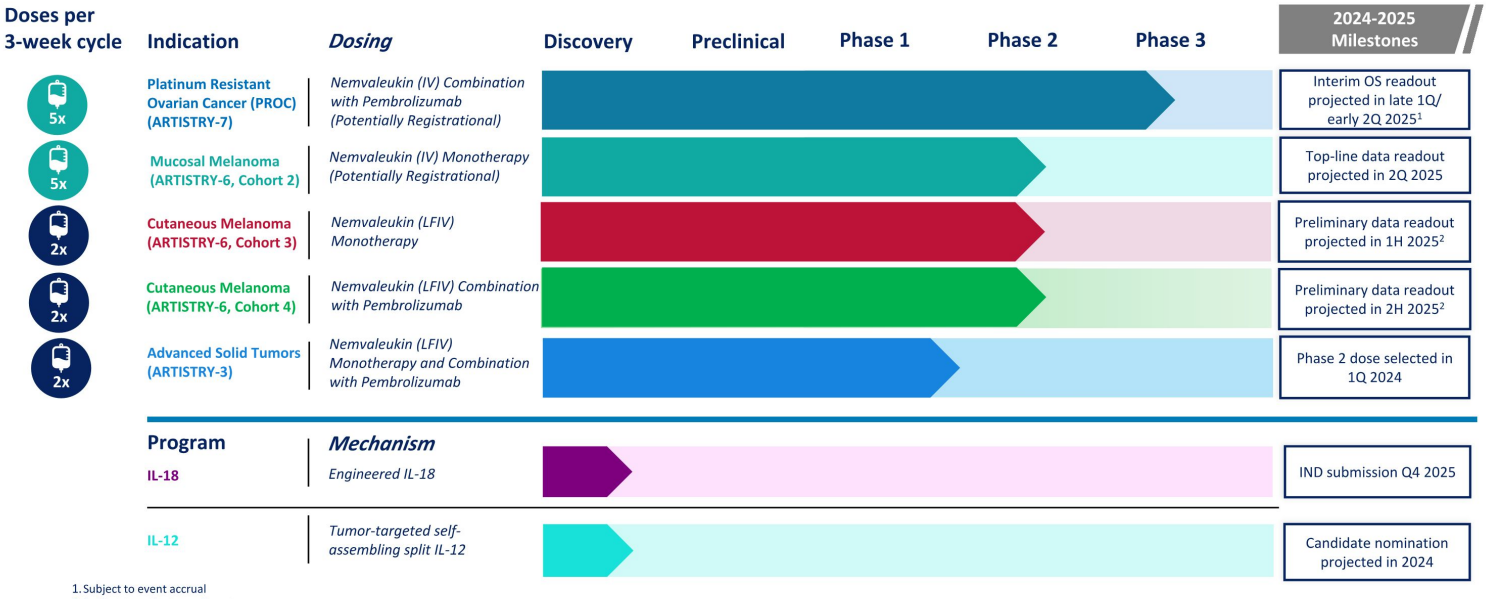
- Elegantly engineered with an 'alpha-non-alpha' structure to mitigate HD IL-2's toxicity
- Design also unlocks therapeutic effects through more selective expansion of cytotoxic $CD8^+$ T cells and NK cells

Comprehensive clinical dataset from Ph1/2 trial (ARTISTRY 1), including deep and durable responses

- Durable responses seen with monotherapy in post PD-1 cutaneous and mucosal melanoma
- Durable responses, including complete responses, seen in combination therapy with pembrolizumab in heavily pre-treated PROC patients[1]
- Manageable AE profile allows administration in outpatient setting. No capillary leak syndrome observed
- Currently in two registrational studies – mono and combination therapy

1. Data available on slide 15 of this presentation
2. ARTISTRY-7 (combination therapy), ARTISTRY-6, cohort 2 (monotherapy)

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

Today's Agenda

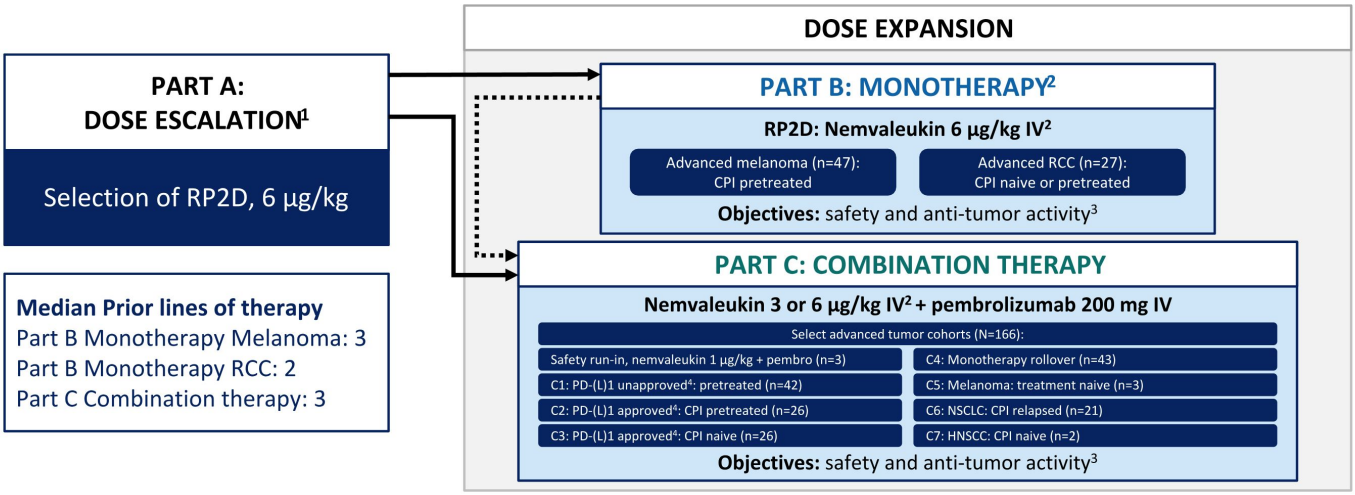
Nemvaleukin clinical proof of concept Monotherapy and combination therapy across broad range of solid tumors	**Ulka Vaishampayan, MD** University of Michigan
Unmet need in platinum-resistant ovarian cancer Current treatment options and gaps	**John Hays, MD, PhD** The Ohio State University
ARTISTRY-7 overview: PROC Trial design, powering assumptions, progress update	**Vicki Goodman, MD** Mural's Chief Medical Officer
Mucosal melanoma and the need for dedicated treatments Differences of disease and current standard of care	**Rich Carvajal, MD** Northwell Health Cancer Institute
ARTISTRY-6 overview: mucosal melanoma Trial design, powering assumptions, progress update	**Vicki Goodman, MD** Mural's Chief Medical Officer
Engineered IL-18 program Protein engineering and early data generation	**Jean Chamoun, PhD** Mural's Vice President, Research
Conclusion and Q&A	**Caroline Loew, PhD and team**

ULKA VAISHAMPAYAN, MD
UNIVERSITY OF MICHIGAN

NEMVALEUKIN ALFA: CLINICAL PROOF OF CONCEPT

MURAL ONCOLOGY

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



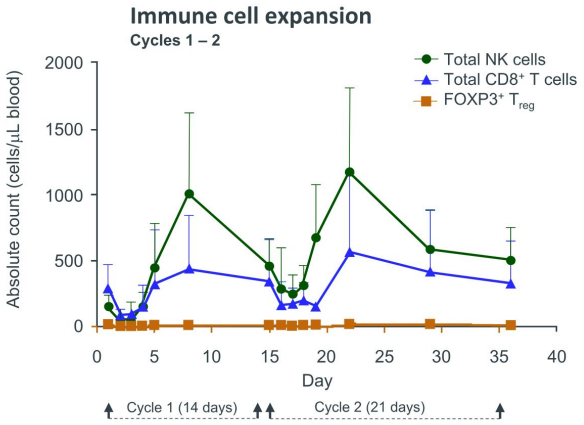
NCTO2799095
1. Patients from Parts A and B could roll over to Part C upon progression or stable disease (after ≥ 4 cycles) on monotherapy
2. Nemvaleukin daily Q5D, then off treatment for 9 days (cycle 1) or 16 days (cycle 2+)
3. ORR assessed by investigator (RECIST v1.1)
4. Nemvaleukin 3 µg/kg/d in C1-C4, 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

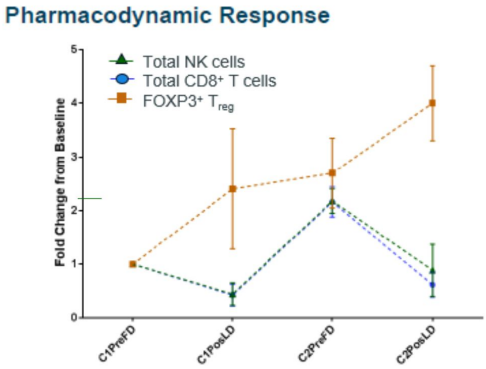
MURAL ONCOLOGY

Clinical Pharamacodynamic Effects of Nemvaleukin are Distinct from HD IL-2, Preferentially Expanding Only Cytotoxic CD8+ T Cells and NK Cells

Nemvaleukin[1]



High-Dose IL-2[2]



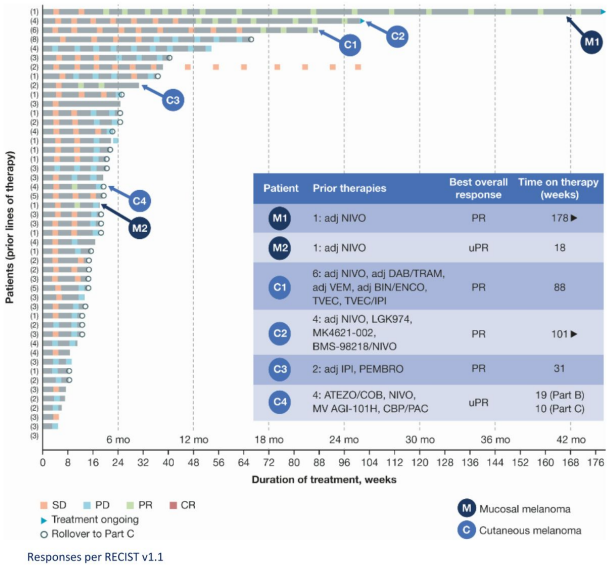
High-dose IL-2 33 µg/kg IV TIDx5

Nemvaleukin: CD8⁺ T and NK cells preferentially expanded 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

MURAL ONCOLOGY

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) Median (range)	40.77 (55.6) [c] 16.75 (6.1-150.3)	78.2 (101.9)[d] 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

Case Study: 66-Year-Old Female with Urethral Melanoma (1 of 2) M1

Dx
Melanoma

- Dx w primary urethral mucosal melanoma in Apr 2017
- Cystectomy & pelvic node dissection in Jun 2017

Prior Treatment

- Adjuvant nivolumab (Sep 2017 – Sep 2018)
- Recurrence 8 months after treatment completion
- Most recent disease progression: Sep 2019

Nemvaleukin Treatment

Artistry 1: October 2019 – termination of study (~44 mo)

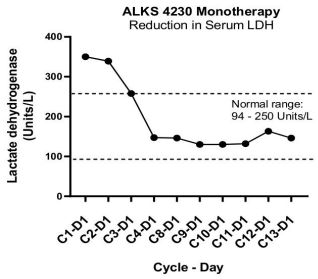
Continuing treatment on EAP as of July 2024 (~57 months from Artistry-1 treatment start)

- Nemvaleukin therapy
- 6 µg/kg IV Nemvaleukin

Target Lesions (Axis mm)		Non-Target Lesions		
Lymph Node Retroperitoneal (31)	Lymph Node L iliac (18)	Lymph node iliac	Lymph node pelvic	Lymph node Retroperitoneal

On-Study Benefits

Change in Target Lesions from Baseline+	
Cycle 2	Stable Disease (SD): 8% increase
Cycle 4	SD: 17% reduction
Cycle 6-55	**Partial Response (PR)+:** 54% reduction at the time of study completion



Notable treatment-related AEs

- Immune-related SAE: Grade 2 iritis/vitritis treated w steroid eye drops
- Grade 3 transient hypotension managed w fluids (SAE)
- Grade 3/4 Neutropenia

+ per RECIST criteria

Artistry-1 Data cut off Aug 2, 2023, EAP cut-off July 2024

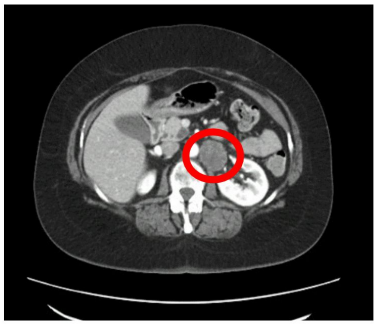
MURAL ONCOLOGY

Case Study: 66-Year-Old Female with Urethral Melanoma (2 of 2): Target Lesion Shrinkage

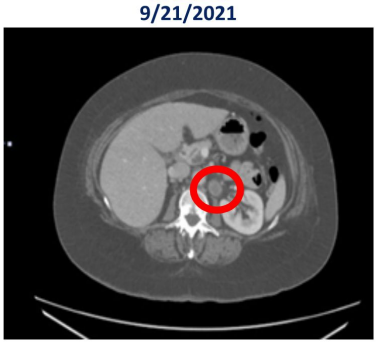
M1

1 of 2 target lymph node lesions

SCREENING 10/9/2019



CYCLE 16 9/21/2021

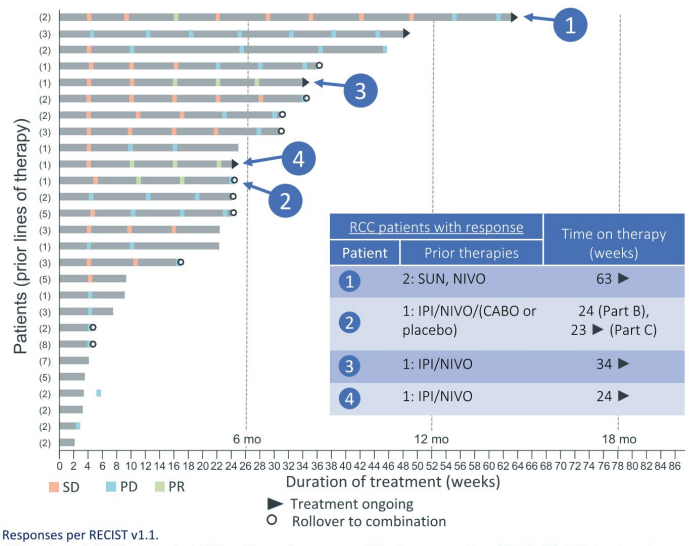


Artistry-1 Part B, melanoma cohort. Data cutoff Aug 2, 2023

EAP study
Data cutoff July 2024

MURAL ONCOLOGY

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



	RCC (n=22)[a]
Best overall response, n (%)	
CR	0
PR	4 (18.2)[b]
ORR, n (%) [95% CI]	4 (18.2) [5.2-40.3]
Median DOR,[c] weeks (range)	15.6 (12.3-39.0)

[a] N= 27 (56% received prior CPI), however 5 patients did not meet tumor-evaluable criteria [b]Includes 3 confirmed PRs and 1 unconfirmed PR. [c]DOR is for Part B only and does not include rollover to Part C; some patients may still be on treatment.

- Clinically meaningful responses observed
- All responders had been on prior CPI therapy and progressed

Data cut off Oct 29, 2021

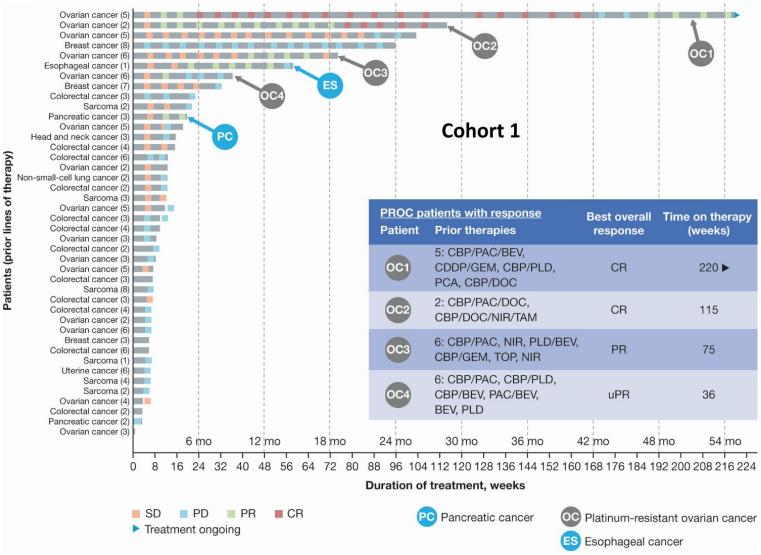
Responses per RECIST v1.1.

CABO, cabozantinib; CPI, checkpoint inhibitor; CR, complete response; DCR, disease control rate (CR+PR+SD); DOR, duration of response; IPI, ipilimumab; mo, months; NIVO, nivolumab; ORR, overall response rate (CR+PR); PD, progressive disease; PR, partial response; RCC, renal cell carcinoma; SD, stable disease; SUN, sunitinib.

1. Vaishampayan U et al. Poster presented at the ASCO Meeting, Chicago, IL, June 3 - 7, 2022

MURAL ONCOLOGY

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



PROC patients with response			
Patient	Prior therapies	Best overall response	Time on therapy (weeks)
OC1	5: CBP/PAC/BEV, CDDP/GEM, CBP/PLD, PCA, CBP/DOC	CR	220 ▶
OC2	2: CBP/PAC/DOC, CBP/DOC/NIR/TAM	CR	115
OC3	6: CBP/PAC, NIR, PLD/BEV, CBP/GEM, TOP, NIR	PR	75
OC4	6: CBP/PAC, CBP/PLD, CBP/BEV, PAC/BEV, BEV, PLD	uPR	36

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

Case Study: 48-Year-Old Female with High-Grade Serous Ovarian Cancer

OC1

Dx in Aug 2014
High Grade Serous Ovarian Cancer

- PD-L1 status: TPS = 20%
- BRCA status: *wild-type*
- HRD status: Proficient
- TMB Intermediate
- MSS
- Platinum-Resistant

Prior Treatment

Line	Therapy	Duration (mos)	Best Response
1	CBP/TAXOL®/AVASTIN®	5	SD
2	CDDP/GEM	4.6	SD
3	CBP/DOXIL®	4.6	SD
4	ABRAXANE®	3.8	SD
5	CBP/TAXOTERE®	4.6	PR

Last dose of prior treatment Feb 22, 2018

ARTISTRY-1 Treatment

Jan. 7, 2019 – termination of study (On treatment ~52 months)*

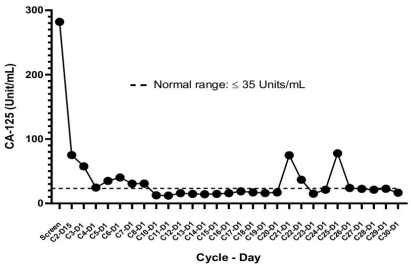
- Nemvaleukin + pembrolizumab therapy
- 3 µg/kg IV Nemvaleukin

Target Lesions (Axis mm)	Non-Target Lesions
L common iliac lymph node (20)	Retroperitoneal lymph node

On-Study Benefits

Change in Target Lesions from Baseline	
Cycle 2	Stable Disease (SD)
Cycle 4	Partial Response+ (PR): 60% reduction **Normalization of CA-125**
Cycle 6	Confirmed PR+
Cycle 8	**Complete Response (CR)+Ŧ:** 60% reduction
Cycle 10-52	**Confirmed (CR)+Ŧ:** 70% reduction

Nemvaleukin + Pembrolizumab Normalization of CA-125 tumor marker



- Tolerated therapy well – no notable treatment-related AEs
- No SAEs reported

BEV=bevacizumab, CBP=carboplatin, CDDP=cisplatin, GEM=gemcitabine.

Data cut off Aug 2, 2023

MURAL ONCOLOGY

Case Study: 83-Year-Old Female with High-Grade Serous Ovarian Cancer

OC2

Dx Oct 2008
High Grade Serous Ovarian Cancer

- PD-L1 status: *unknown*
- BRCA status: *wild-type*
- HRD status: unknown
- TMB status: unknown
- Micro-satellite unknown
- Platinum-Resistant

Prior Treatment

Line	Therapy	Duration (mos)	Best Response
1	CBP/TAXOL*/TAXOTERE*	4	Not Evaluable
2	CBP/ZJL/TAM/TAXOTERE*	6	CR

Last dose of prior treatment Dec 7, 2018

ARTISTRY-1 Treatment

Feb 2020 – April 2022 (On treatment ~26+ months)

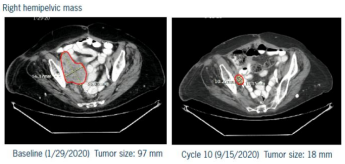
Nemvaleukin + pembrolizumab therapy

3 µg/kg IV Nemvaleukin

Target Lesions (Axis mm)		Non-Target Lesions
R hemi-pelvic mass (97)	R retroperitoneal nodule (34)	None

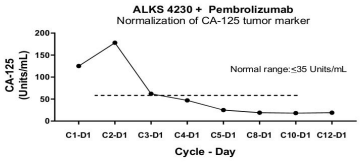
> 80% decrease in target lesion in right pelvis

A. Right hemipelvic mass



Baseline (1/29/2020) Tumor size: 97 mm

Cycle 10 (9/15/2020) Tumor size: 18 mm



On-Study Benefits

Change in Target Lesions from Baseline	
Cycle 2	Stable Disease (SD): 6% reduction
Cycle 4	Partial Response (PR)+: 55% reduction
Cycle 6	**Confirmed PR+**: 68% reduction
Cycle 8-22	PR+: 76-95% reduction
Cycle 24-32	Complete Response (CR): 100% reduction

D/C study due to pt death (due to colonic perforation not related to study treatment)

Notable treatment-related AEs

- Grade 3 neutropenia

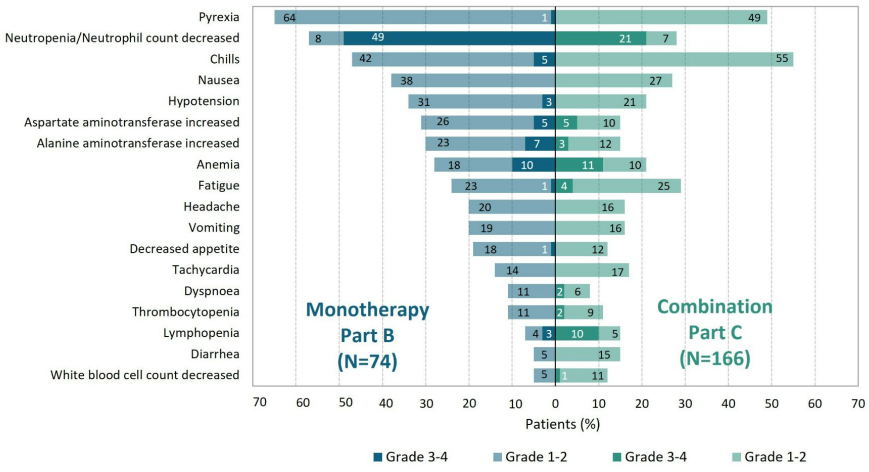
+per RECIST criteria.

Data cut off Aug 2, 2023

MURAL ONCOLOGY

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

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 on file.

- 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]

JOHN HAYS, MD, PHD
THE OHIO STATE UNIVERSITY
COMPREHENSIVE CANCER CENTER

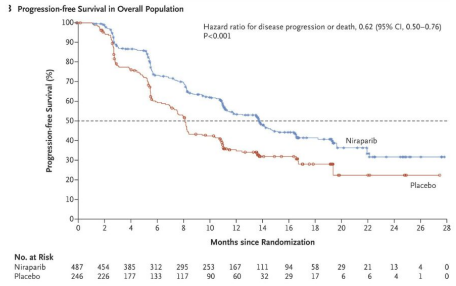
UNMET NEED IN PLATINUM-RESISTANT OVARIAN CANCER

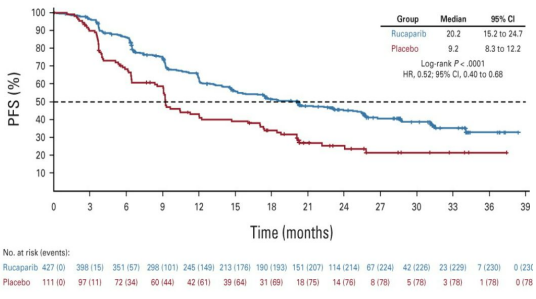
MURAL ONCOLOGY

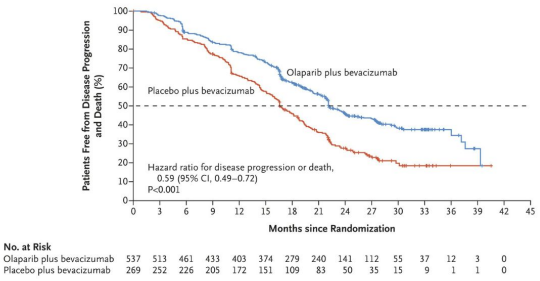
•. 2023 Jan 20;41(3):609-617

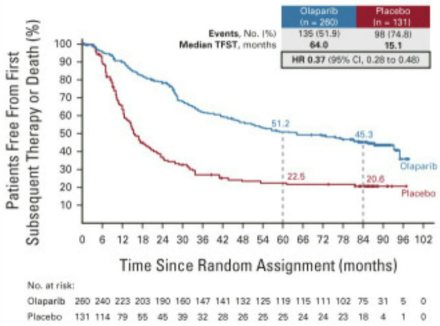
Platinum Resistant Ovarian Cancer (PROC)

- Ovarian cancer is the second most common gynecologic malignancy but most common cause of gynecologic cancer death in US (~20-25K cases per year)
- No commonly agreed upon early detection test
- 75% of patients diagnosed at advanced stage (Stage III-IV)
  - Primary treatment is systemic chemotherapy/surgery ± maintenance therapy



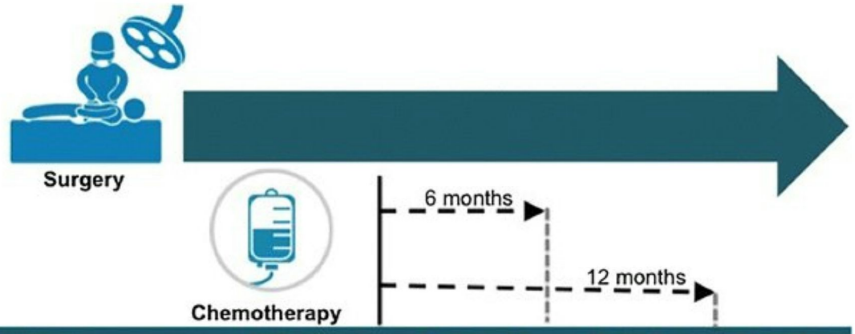






Clockwise from top left: Gonzales Martin et al N Engl J Med 2019;381:2391-2402; Monk et al JCO 2022; 40(34):3952-3964; Ray-Coquard et al N Engl J Med 2019;381:2416-2428; DiSilvestro et al JCO 2023 Jan 20;41(3):609-617

What do we do when patients recur?



Platinum sensitivity classification	Refractory	Resistant	Partially sensitive	Sensitive
Probability of second platinum response	0%	<10%	30%	>50%

Oronsky et al Med Onc 2017 Med Oncol 2017 Jun;34(6):10

Platinum Resistance

- Almost all patients who recur will become platinum resistant…
- Aurelia
  - Chemotherapy w/wo bevacizumab
  - Improved PFS but not OS

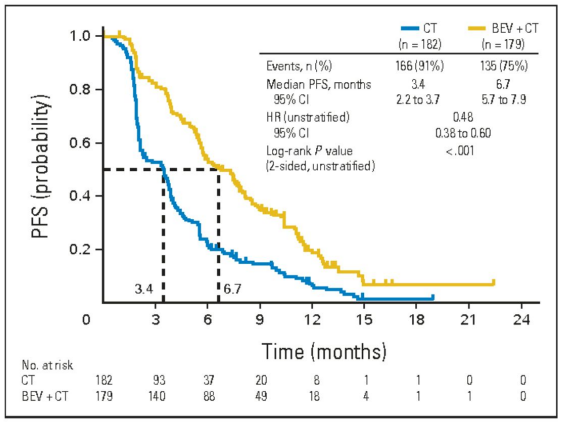


Fig 2. Progression-free survival (PFS). BEV, bevacizumab; CT, chemotherapy; HR, hazard ratio.

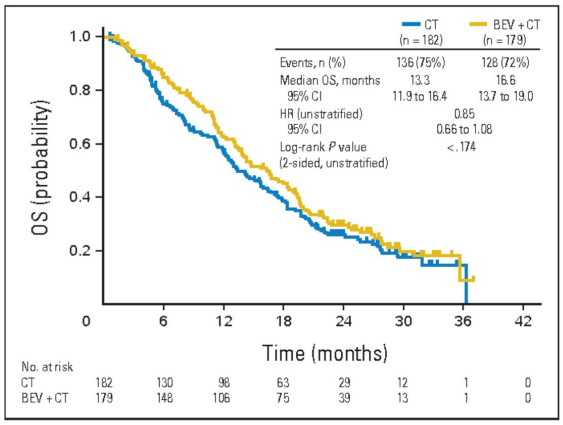


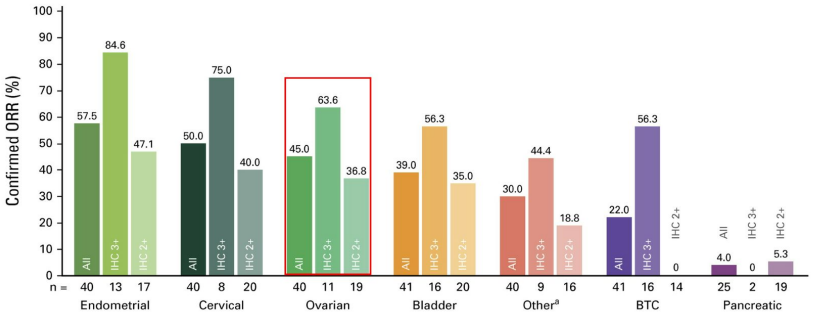
Fig 3. Overall survival (OS). BEV, bevacizumab; CT, chemotherapy; HR, hazard ratio.

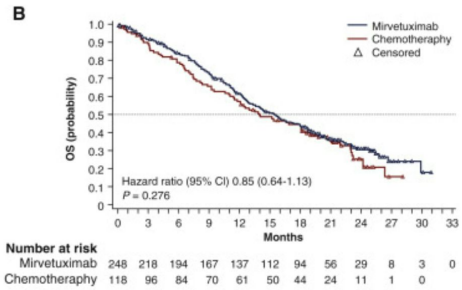
Pujade-Loraine JCO 2014 May 1;32(13):1302-8

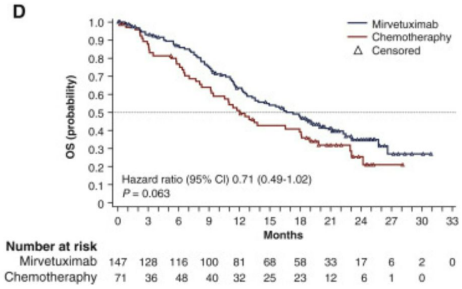
What about the last 10 years?

Antibody Drug Conjugates

- Two new approvals in last 2 years
  - Mirvetuximab Sorevtansine (FRα)
  - Trastuzumab Deruxtecan (HER2)







Moore et al Annals of Oncology Volume 32, Issue 6, June 2021, Pages 757-765

Meric Burnstam et al JCO 2024 Jan 1:42(1):47-58.

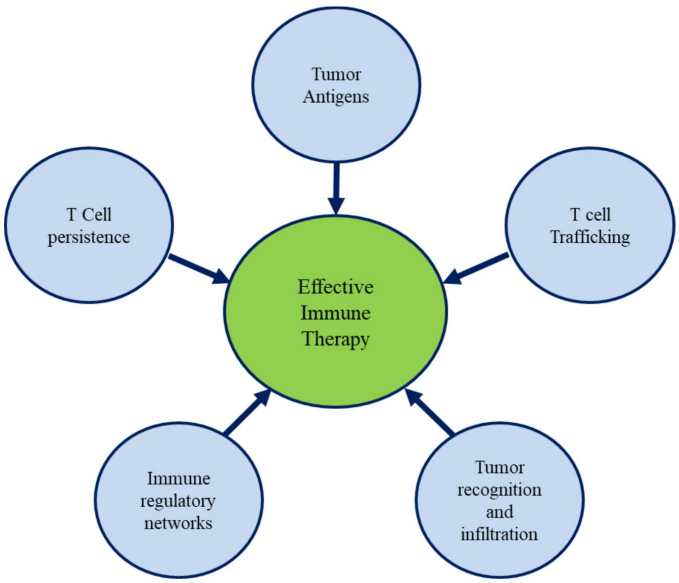
What about the last 10 years?

Many agents tested:

- Immune therapy
    - Checkpoint inhibitors (PD1/PD-L1, CTLA4, TIGIT, etc…)
    - Novel antigen delivery/recognition (NY-ESO, CA125)
    - Bispecific T-Cell Engagers (BiTE)
    - CAR-T/TCR
- Underwhelming performance
    - 10-15% RR for single agents
    - Increased for combinations (e.g. PD-L1/CTLA4) but at increased toxicity cost

What About the Future?

- ADCs are great, but…
  - Limited population with marker
    - FRα high – 30-60%
    - HER2 2/3+ – 30%
- IO therapy has promise but monotherapy has limitations
    - Smart combinations are the way forward

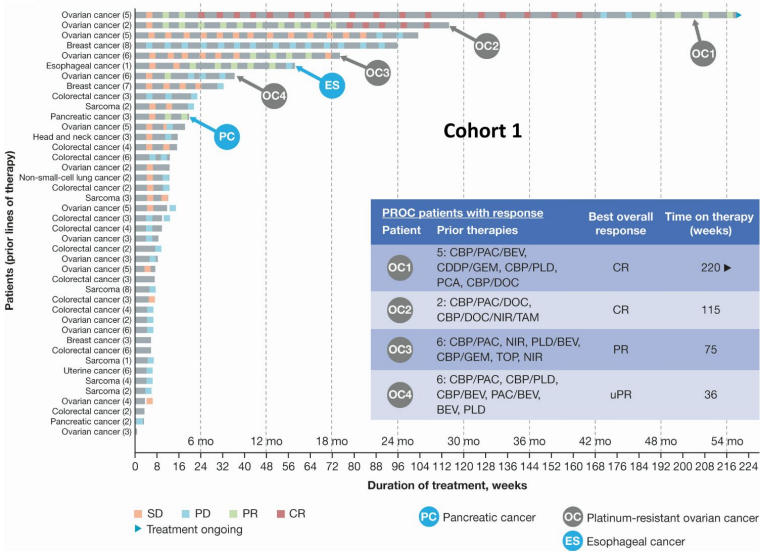


VICKI GOODMAN, MD
CHIEF MEDICAL OFFICER

ARTISTRY-7 OVERVIEW

MURAL ONCOLOGY

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



PROC patients with response			
Patient	Prior therapies	Best overall response	Time on therapy (weeks)
OC1	5: CBP/PAC/BEV, CDDP/GEM, CBP/PLD, PCA, CBP/DOC	CR	220 ▶
OC2	2: CBP/PAC/DOC, CBP/DOC/NIR/TAM	CR	115
OC3	6: CBP/PAC, NIR, PLD/BEV, CBP/GEM, TOP, NIR	PR	75
OC4	6: CBP/PAC, CBP/PLD, CBP/BEV, PAC/BEV, BEV, PLD	uPR	36

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

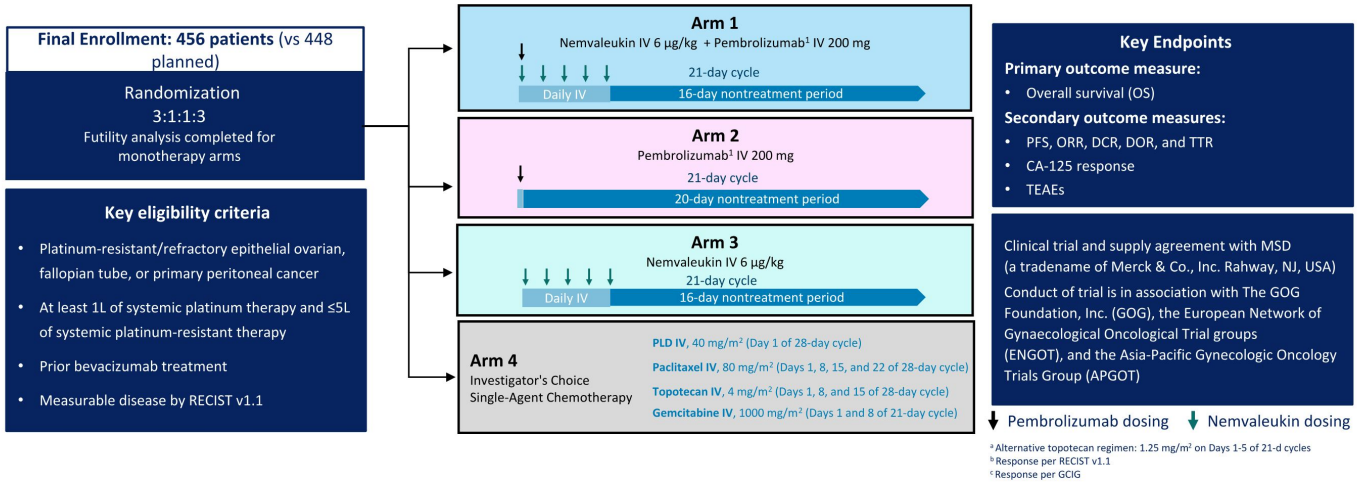
Data cut off Mar 27, 2023
1. DOR data cut off Sept 27, 2023

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

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

Investigational Nemvaleukin IV + Pembrolizumab versus Chemotherapy



[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

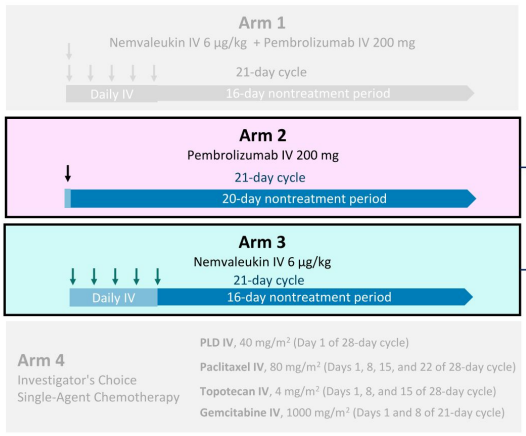
1. Pembrolizumab may be administered up to 35 cycles.

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: 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:

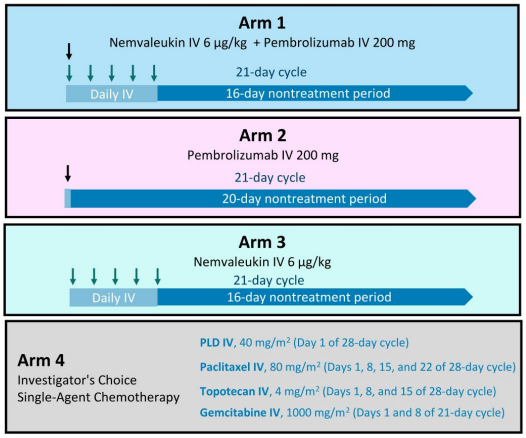
- Based on two phase 2 trials using different doses and schedules of aldesleukin with consistent response rates of approx. 25%, including some patients with durable CRs[1]
- At least 1 patient among first 24 enrolled to achieve ORR or SD for at least 3 months needed to continue enrollment
- **Nemvaleukin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

ARTISTRY-7: Enrollment and Statistical Assumptions



Final Enrollment

~187

27

55

~187

456 patients

Final Enrollment Across Experimental Arms:

- 374 patients enrolled (approximately 187 per arm)
- Enrollment stratified by PD-L1 expression levels, histological subtype, and choice of chemotherapy

Overall Survival Expectations and Rationale:

- OS will be the only hypothesis tested endpoint, with alpha controlled at 2.5% (one sided)
- Expected OS benchmarked using several historical phase 3 trials:
  - Studies differed in eligibility, particularly concerning lines of prior therapy, and with respect to our study
  - Most allowed </= 3 prior lines of therapy and had median OS on chemo control arm between 8 and 13 months
- **Protocol assumptions are a median OS of 10 months for chemotherapy arm and median OS of 14.3 months for Arm 1 (nemvaleukin + pembrolizumab)**

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 interim analysis is 1-sided, 0.0096

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

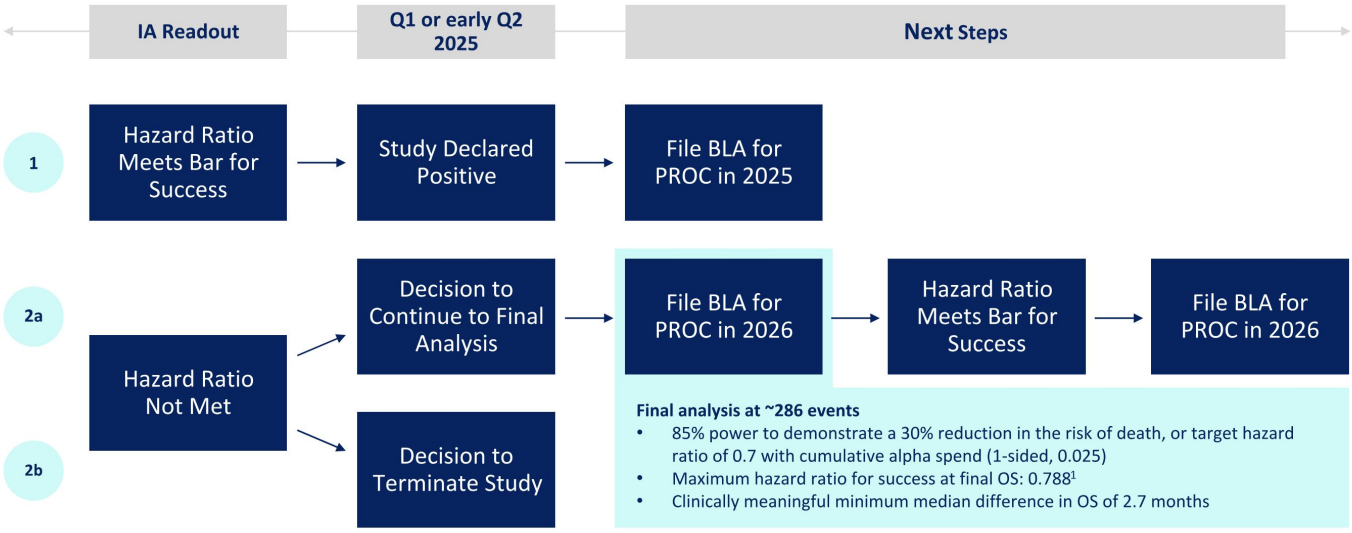
TIMING

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

ARTISTRY-7 Interim Analysis (IA): Potential Outcomes



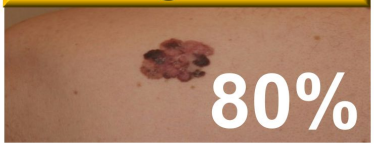
RICH CARVAJAL, MD
NORTHWELL HEALTH CANCER INSTITUTE

MUCOSAL MELANOMA & THE NEED FOR DEDICATED TREATMENTS

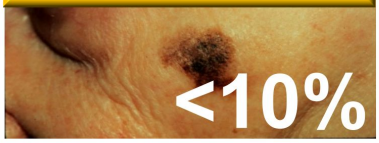
MURAL ONCOLOGY

Mucosal Melanoma: A Rare Melanoma Subtype

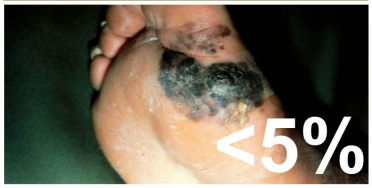
Melanoma in Non-Sun Damaged Skin



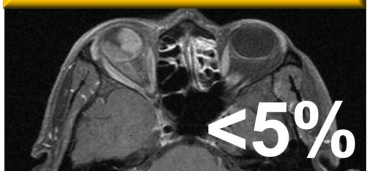
Melanoma in Sun Damaged Skin



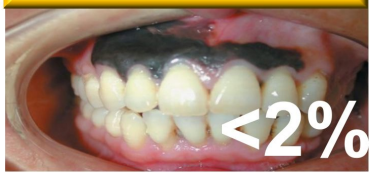
Acral Melanoma



Uveal Melanoma



Mucosal Melanoma



Conjunctival Melanoma

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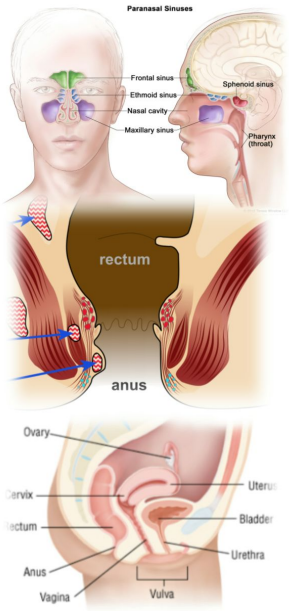
The Clinical Heterogeneity of Mucosal Melanoma

Head and Neck Mucosa (55%)

- **Location**
  - Nasal Cavity, 49%
    - Lateral nasal wall
    - Turbinates
  - Paranasal Sinuses, 10%
    - Maxillary sinus
    - Ethmoid sinus
  - Oral Cavity, 41%
    - Hard palate
    - Upper alveolus
- **Symptoms**
  - Sinonasal: Nasal obstruction, epistaxis, loss of smell, pain, proptosis, diplopia
  - Oral Cavity: Bleeding, ulceration, discoloration, ill-fitting dentures



Anorectal Mucosa (24%)

- **Location**
  - Anal Canal, 33%
  - Anorectal, 25%
  - Rectal, 42%
- **Symptoms**
  - Rectal bleeding, painful defecation, anorectal masses, "hemmorrhoids"

Vulvovaginal Mucosa (18%)

- **Location**
  - Vulvar, 90%
  - Vaginal, 10%
- **Symptoms**
  - Vulvar: Pruritis, bleeding, ulceration
  - Vaginal: Vaginal discharge, dysparenuria, vaginal mass

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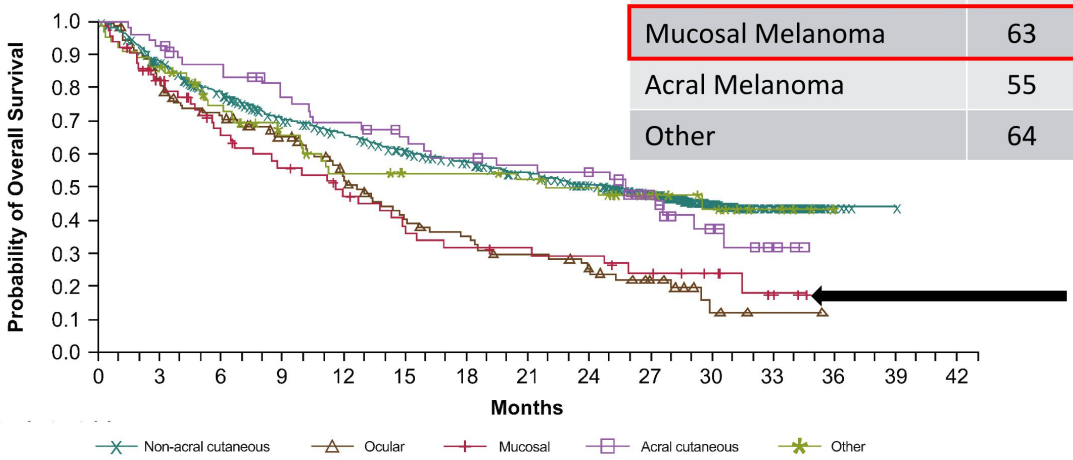
Carvajal RD et al. JNCCN 2012.
Prasad et al. Head and Neck 2006.

CheckMate 172 (n=1008): OS with Nivolumab by Subtype

Subtype	n	Median OS (mos)
Non-Acral Cut Melanoma	723	25.3 (95% CI, 20.9 – 28.9)
Ocular Melanoma	103	12.6 (95% CI, 10.2 – 15.1)
Mucosal Melanoma	63	11.5 (95% CI, 6.4 – 15.0)
Acral Melanoma	55	25.8 (95% CI, 15.1 – 30.6)
Other	64	21.8 (95% CI, 9.8 – NR)



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Nathan et al, Eur J of Ca 2019.

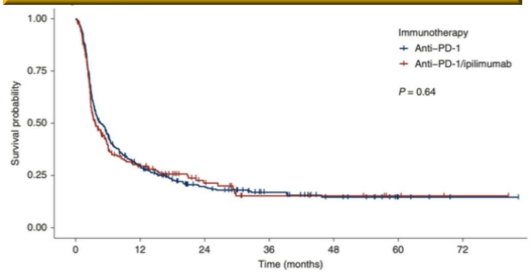
International Real World Data Experience (n = 545)

- Data on patients from 25 centers in Australia, Europe, USA and Asia
- Median follow-up of 31 months (95% CI, 17-54)

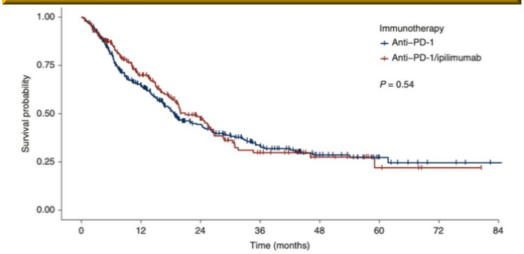
Table 4. ORR by primary site, Ethnicity/Race and systemic treatment.

		Overall n/N %	Ethnicity/Race		Treatment	
			Caucasian	Asian	Anti-PD1	AntiPD1/Ipilimumab
Overall ORR n/N %		162/545 (30)	101/331 (31)	47/176 (27)	100/348 (29)	62/197 (31)
ORR by primary site n/N % (95% CI)	Anorectal	38/116 (33)	27/81 (33)	6/25 (24)	22/70 (31)	15/46 (33)
	Urogenital	47/178 (26)	34/124 (27)	8/41 (20)	31/104 (30)	17/74 (24)
	Naso-oral	66/206 (32)	36/115 (31)	26/79 (33)	40/140 (29)	26/66 (40)
	Other	11/45 (24)	4/11 (36)	7/31 (23)	7/34 (21)	4/11 (36)
ORR by race n/N % (95% CI)	Caucasian	-	-	-	58/191 (31)	43/140 (32)
	Asian	-	-	-	37/146 (26)	10/30 (34)
PFS	Median, months (95% CI)	4 (4 - 6)	5 (4 - 6)	4 (3 - 6)	5 (4 - 6)	4 (3 - 6)
	3-year rate % (95% CI)	17 (13 - 21)	16 (12 - 21)	18 (13 - 26)	17 (13 - 22)	16 (10 - 25)
OS	Median , months (95% CI)	19 (18 - 24)	21 (18 - 26)	18 (15 - 27)	19 (16 - 24)	21 (19 - 27)
	3-year rate % (95% CI)	32 (27 - 37)	33 (27 - 40)	32 (24 - 43)	33 (27 - 39)	30 (22 - 40)

Progression-Free Survival



Overall Survival



Dimitriou F et al. Ann Oncol, 2022.

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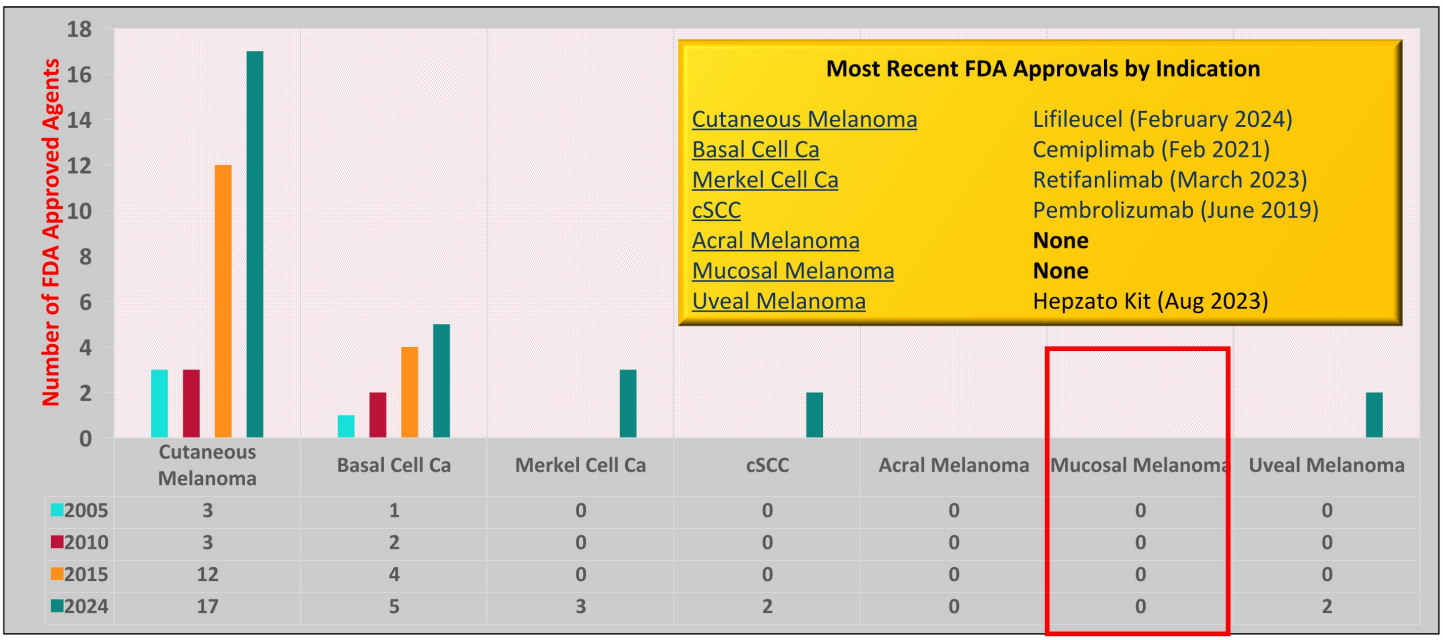
FDA Approvals for Melanoma and Cutaneous Malignancies



	Cutaneous Melanoma	Basal Cell Ca	Merkel Cell Ca	cSCC	Acral Melanoma	Mucosal Melanoma	Uveal Melanoma
2005	3	1	0	0	0	0	0
2010	3	2	0	0	0	0	0
2015	12	4	0	0	0	0	0
2024	17	5	3	2	0	0	2

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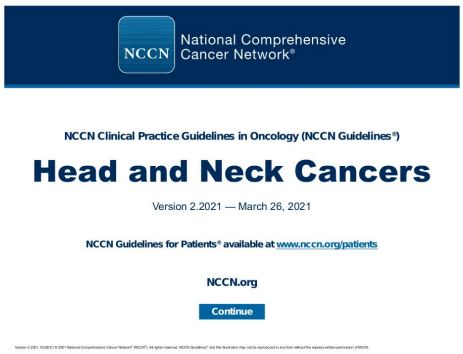
Completed Clinical Trials in Mucosal Melanoma

Setting	Study	Phase	n	Treatment Arm(s)	Results
Neoadjuvant	Mao et al, ASCO 2023	2	19	Lenvatinib + Pembro	32% path RR in resected population (n=15)
	Lian et al, Ann Oncol 2024	2	29	Toripalimab + Axitinib	33% path RR in resected population (n=24)
Adjuvant	**Lian et al, JCO 2013**	**2**	**189**	**Obs vs HDI vs Cis/TMZ**	**RFS and OS improved with Cis/TMZ vs Obs or HDI**
	Lian et al, ASCO 2018	**3**	**204**	**HDI vs Cis/TMZ**	**Primary Endpoint of RFS reached (15.5 vs 9.5 mos) in favor of chemo**
	Lian et al, Ann Oncol 2022	**2**	**145**	**Toripalimab vs HDI**	**Similar RFS (13.6 vs 13.9 mos) and more favorable safety profile in favor of toripalimab**
Metastatic	Sheng et al, JCO 2019; Li S, JITC 2022	1B	33	Toripalimab + Axitinib	48% ORR in chemo-naive patients (n=29); PFS 7.5 mos
	Nomura et al, Int J Clin Onc 2020	2	20	Nivolumab	ORR 23.5% (n=17); PFS 12 mos; 1 yr OS rate 50%
	Yan et al, JCO 2021	**2**	**114**	**Carbo/Taxol +/- Bev**	**Primary Endpoint of PFS reached in favor of bevacizumab (4.8 vs 3.0 mos); OS 13.6 vs 9 mos in favor of bev**
	Mao L, Clin Cancer Res 2022	2	43	Atezolizumab + Bev	ORR 45%, median PFS 9.2 mos, median OS not reached
	Zhao L, JITC 2024	2	32	Camrelizumab + Apatinib	ORR 43%, PSF 8 months

Limited Guidelines Available to Guide Management

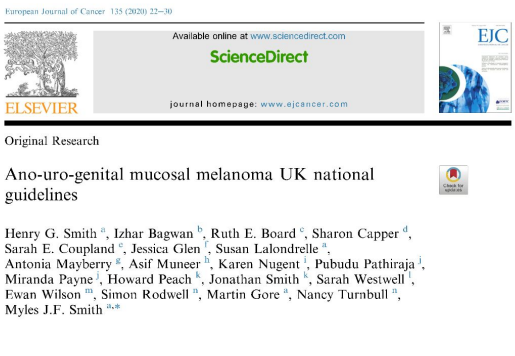
Sinonasal and Oral Cavity Melanoma



NCCN Guidelines, Head and Neck Cancers.

Nenclares et al. Eur J Cancer, 2020.

Anorectal and Vulvovaginal Melanoma



Smith HG et al. Eur J Cancer, 2020.

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How do we manage advanced disease?

1. Appropriate **clinical trial** if available
2. **CPI** as SOC front-line therapy
3. **Targeted therapy** as next line if actionable alteration present
4. **Carbo/Taxol/Bev**
5. Other **chemotherapy** regimens

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Summary

- Mucosal melanoma is a **rare melanoma subset** with a distinct biology and a **particularly poor prognosis**
- There is **no proven effective therapy** in the perioperative or metastatic settings
- Only **limited efforts** are ongoing that are focused on developing novel therapies specifically for mucosal melanoma
- This patient population represents a **significant unmet medical need**

Northwell Health Cancer Institute

VICKI GOODMAN, MD
CHIEF MEDICAL OFFICER

ARTISTRY-6 OVERVIEW

MURAL ONCOLOGY

Systematic Literature Review of Outcomes and Treatments in Post-Anti-PD-(L)1 Advanced Mucosal Melanoma

Systematic Literature Review (SLR) conducted to identify interventional and real-world (RW) studies assessing treatments and clinical outcomes in patients with advanced mucosal melanoma who have previously been treated with anti-PD-(L)1 therapy

11 RW studies

1 interventional study

TREATMENT OVERVIEW

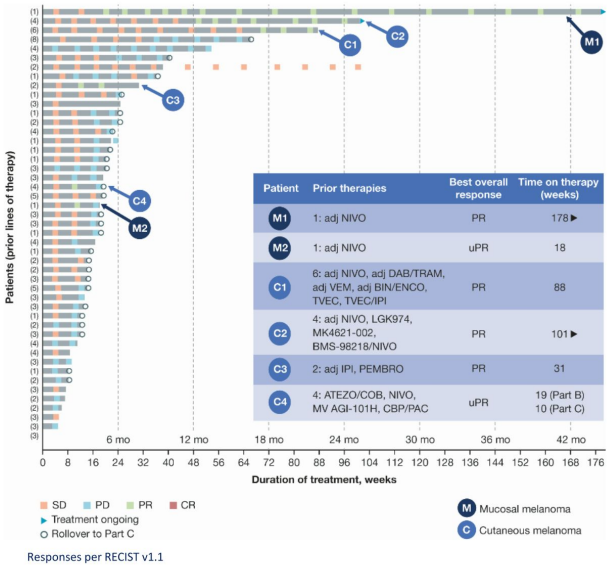
- In the RW studies, post anti-PD-(L)1 treatments included checkpoint inhibitors (e.g., ipilimumab, and/or anti-PD-[L]1 rechallenge), cytotoxic agents, targeted therapies, radiation therapy, best supportive care, and treatments used off label such as tyrosine kinase inhibitors
- No cell therapy was reported in the RW studies
- In the interventional study, the reported post anti-PD-(L)1 treatment was lifileucel monotherapy, a tumor-infiltrating lymphocytes cell therapy

RW ORR Outcomes in Patients with Mucosal Melanoma Post Anti-PD-(L)1

- Four of the 11 RW studies reported ORR
- Each study contained 4-16 patients
- Patients received a variety of agents, including single agent and combination CPIs, kinase inhibitors, and combo CPI/kinase inhibitors
- ORR ranged from 0-25%, the latter in a sample size of 4

1 interventional study included 12 patients treated with lifileucil, a treatment with severe limitations, with a response rate of 50%

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) Median (range)	40.77 (55.6) [c] 16.75 (6.1-150.3)	78.2 (101.9)[d] 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.

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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

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ARTISTRY-6 Cohort 2: Assumptions on Final Data

- 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

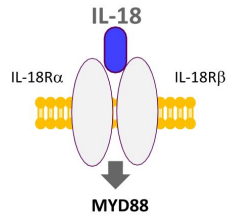
JEAN CHAMOUN, PHD
VICE PRESIDENT, RESEARCH

ENGINEERED IL-18 PROGRAM

MURAL ONCOLOGY

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

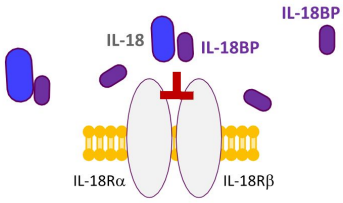
IL-18 Attractive Biology



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

Limited Application

IL-18 Challenges



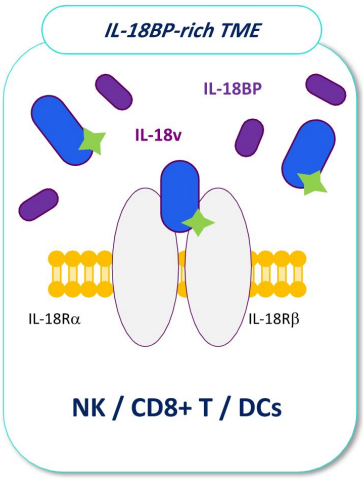
- IL-18BP overexpressed in the TME
- IL-18BP binds strongly to IL-18 minimizing it's signaling
- IL-18 rapidly cleared from circulation

Suppressed activity

MURAL ONCOLOGY

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

Mural Solution: Engineer an IL-18 with Optimized Characteristics

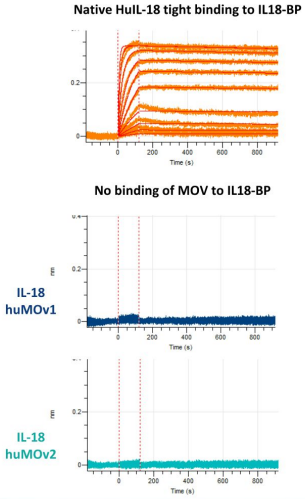


- **Engineer an active IL-18 molecule unaffected by IL-18BP presence**
- **Engineer an IL-18 with and extended half-life**
- **Optimize the IL-18 potency to fit its newly engineered profile**

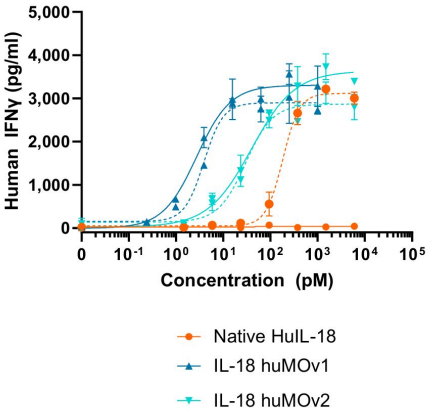
Enhanced Anti-Tumor Activity

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

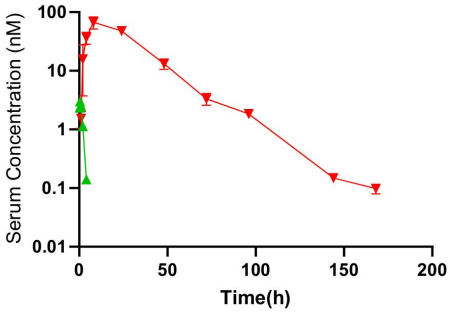


Broad Range of Potency



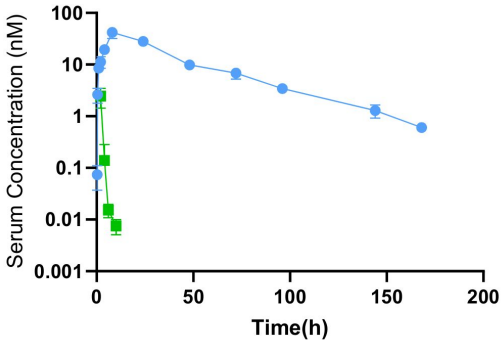
huMOv1/2/3- human Mural Oncology variants
IL18BP-resistant, half-life enhanced

Enhanced Pharmacokinetics



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

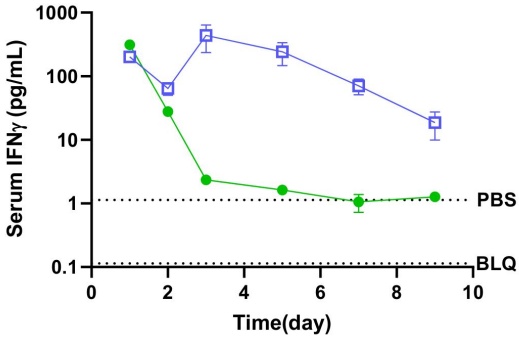
Enhanced Pharmacokinetic



Naked mouse tool variant

muMOv1

Extended Pharmacodynamic

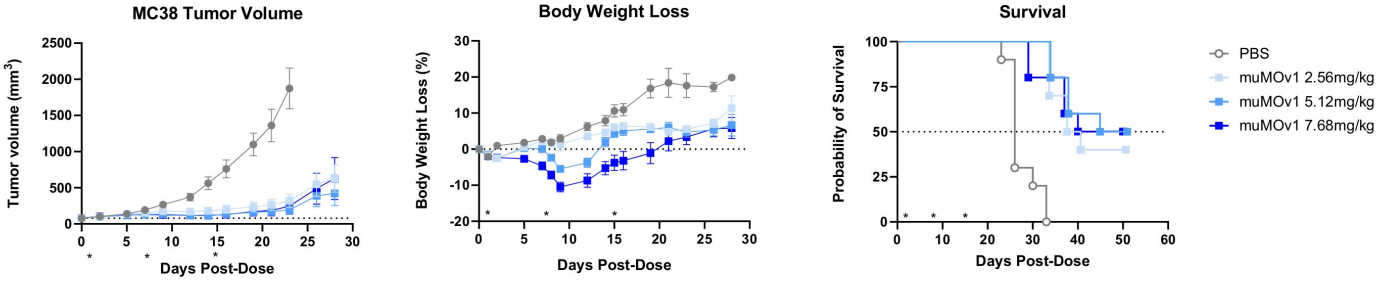


Naked mouse tool variant

muMOv1

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

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

Key Takeaways: IL-18

- Mural's **fit-for-purpose approach** successfully engineered an IL-18 molecule with the desired profile:
  - Maximal resistance to IL18-BP binding
  - Enhance half-life compared to native IL-18
  - Optimized potency

- Clearly demonstrated desired efficacy with mouse ortholog variant

- IND filing by Q4 of 2025

CAROLINE LOEW, PHD

WHY MURAL & WHY NOW?

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

Key Takeaways: ARTISTRY-7 Trial Design Assumptions and Progress

- **Fully enrolled with 456 patients** (versus 448 planned), with approximately 187 patients per experimental arm

- **Futility analysis complete** for monotherapy arms:
  - Pembrolizumab monotherapy arm reached futility (defined as <2 confirmed CR or PR in the first 12 patients) in August 2023 after enrolling 27 patients
  - Nemvaleukin arm required at least 1 patient among the first 24 to achieve a response or SD for at least 3 months to continue; this arm continued to enroll a total of 55 patients

- **Design assumptions on overall survival endpoint**, with alpha controlled at 2.5% (one sided):
  - Chemo arm: estimated median OS of 10 months
  - Nemva + pembro arm: estimated median OS of 14.3 months

Projected readout on 75% of events in late Q1 or early Q2 2025

Key Takeaways: ARTISTRY-6 Cohort 2 Trial Assumptions and Progress

- Cohort 2 or ARTISTRY-6 study expected to provide the **most robust clinical dataset in advanced mucosal melanoma to date**
- **Fully enrolled** with 92 patients
- **Target response rate: 25%**
  - Response rate of 20-25% would be meaningful for patients and would support discussion with FDA around Biologics License Application (BLA)
- Trial designed so that at 25% response rate, lower bound of 95% confidence interval will exceed a 15% response rate
- **Potential for accelerated approval, and discussions with FDA on potential confirmatory evidence package ongoing**
  - Regulatory filing may be deferred if ARTISTRY-7 study continues to final analysis, pending the final outcome of ARTISTRY-7

Projected readout in Q2 2025

Q&A

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